

FIG. 1

b. a. \ominus



\oplus

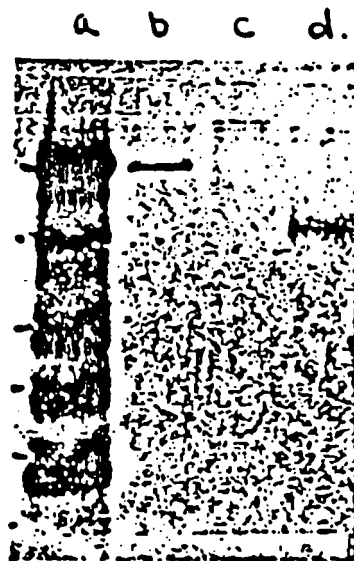


FIG. 3

a b c d.

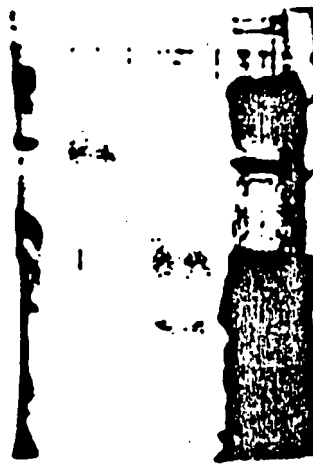


FIG 4

a. b.

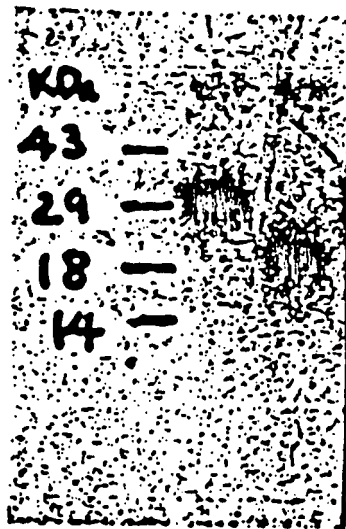
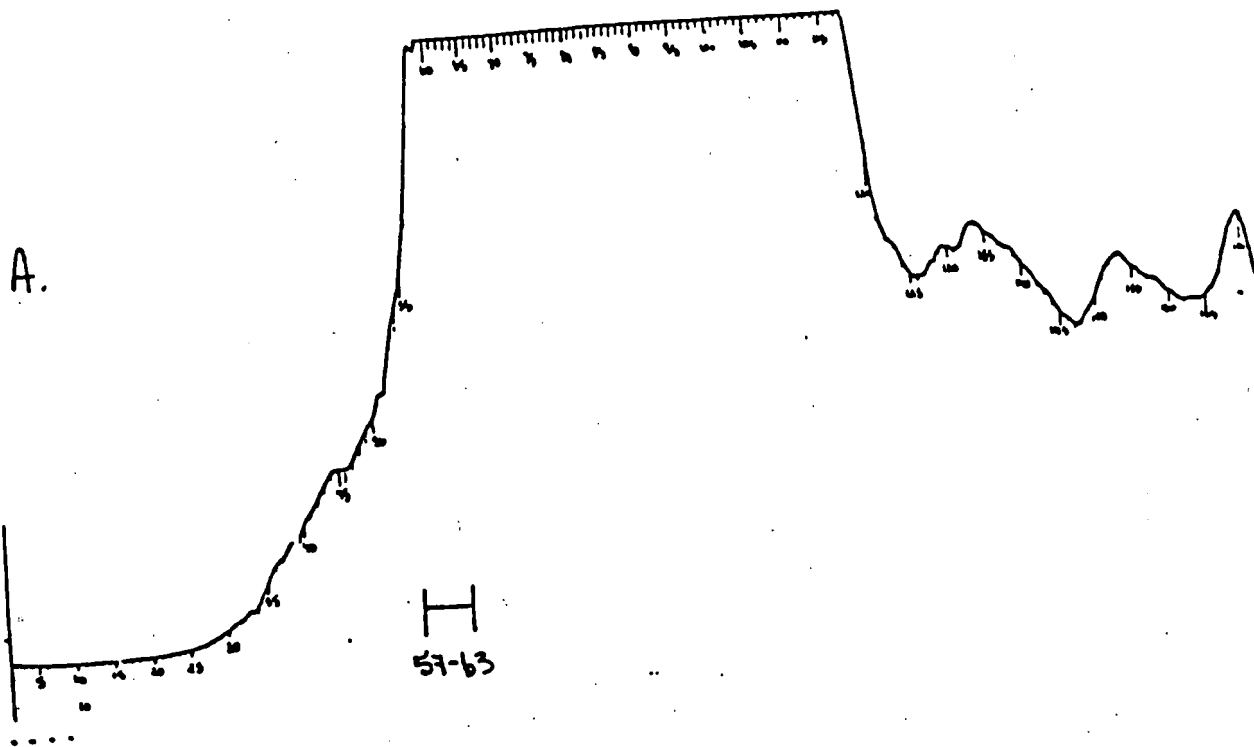


FIG. 5

Figure 6

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B.

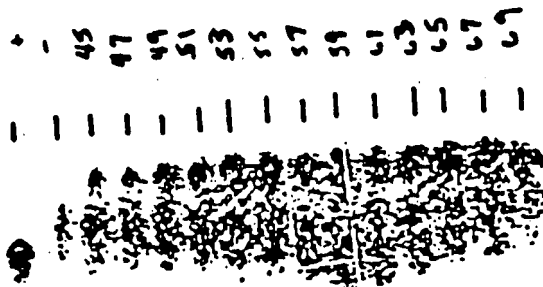
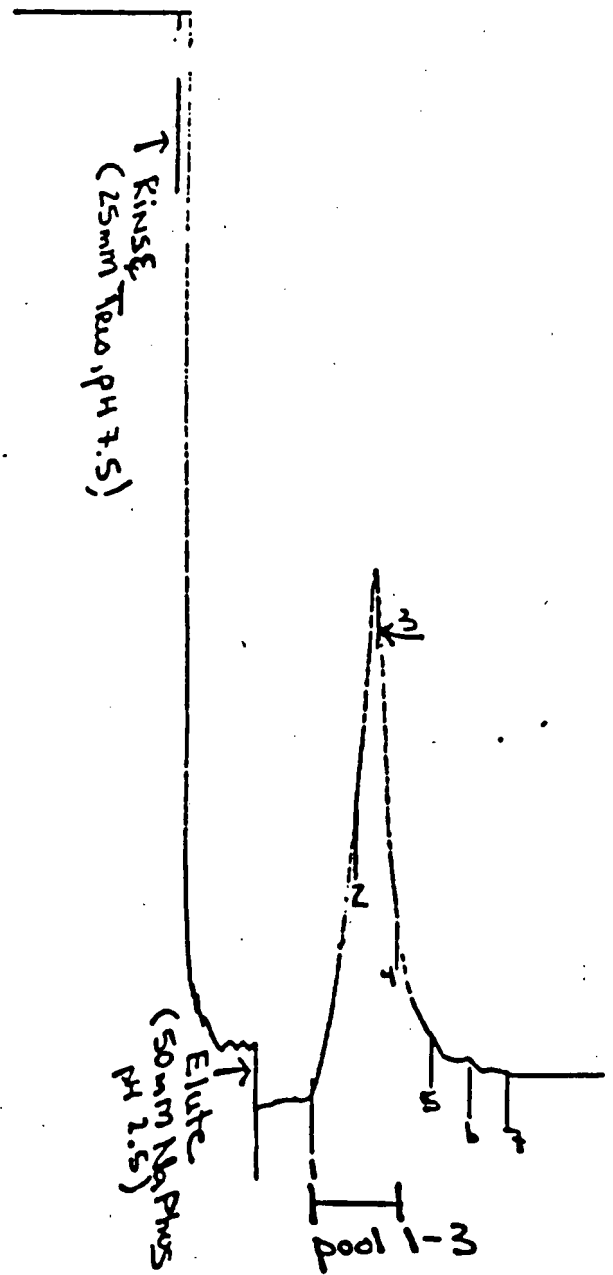


Figure 7



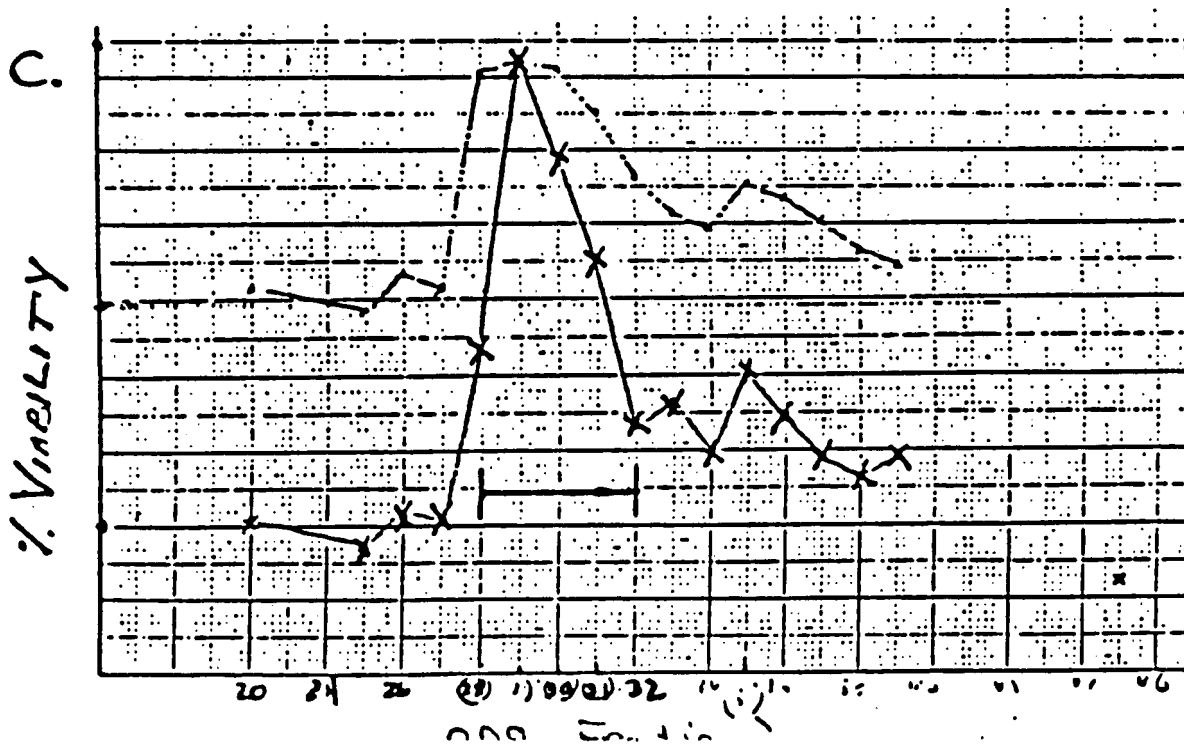
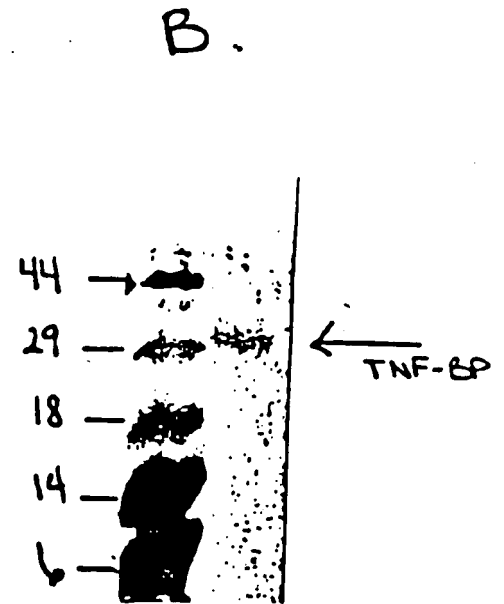
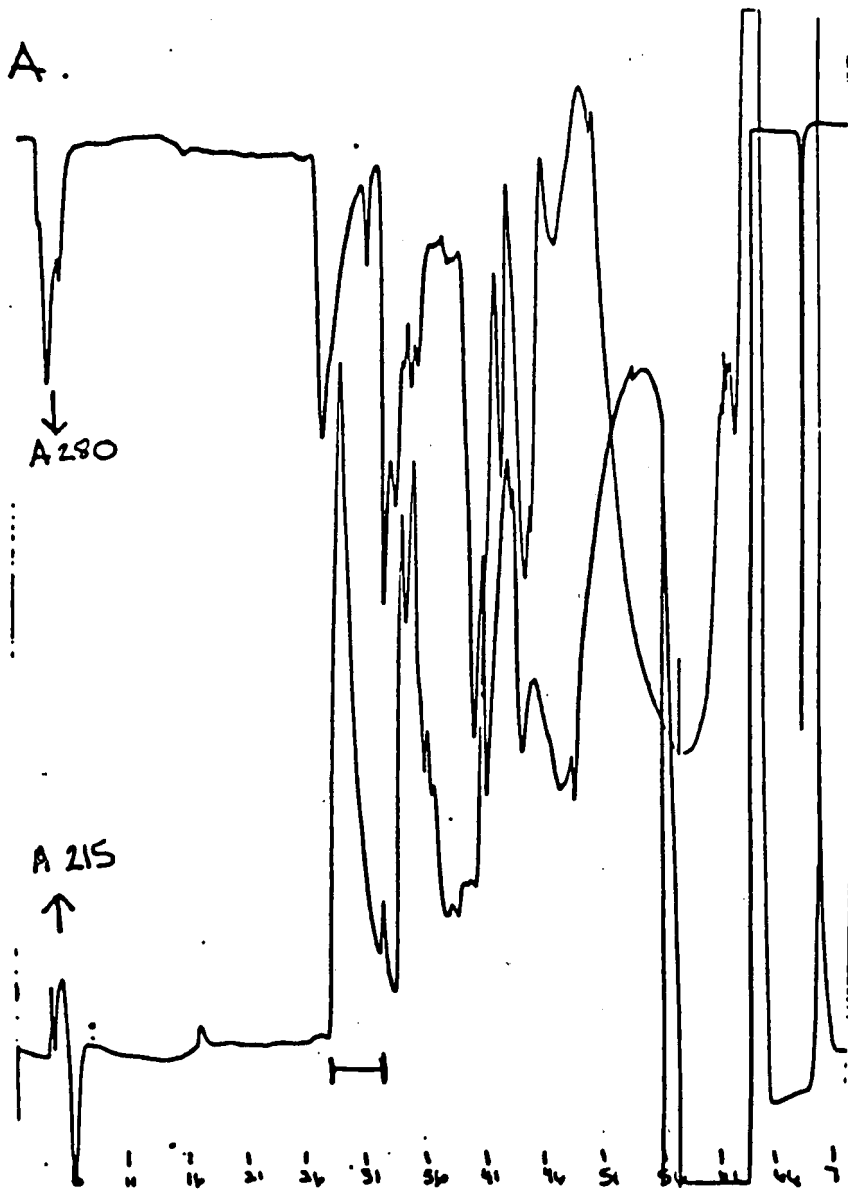


FIG. 9A

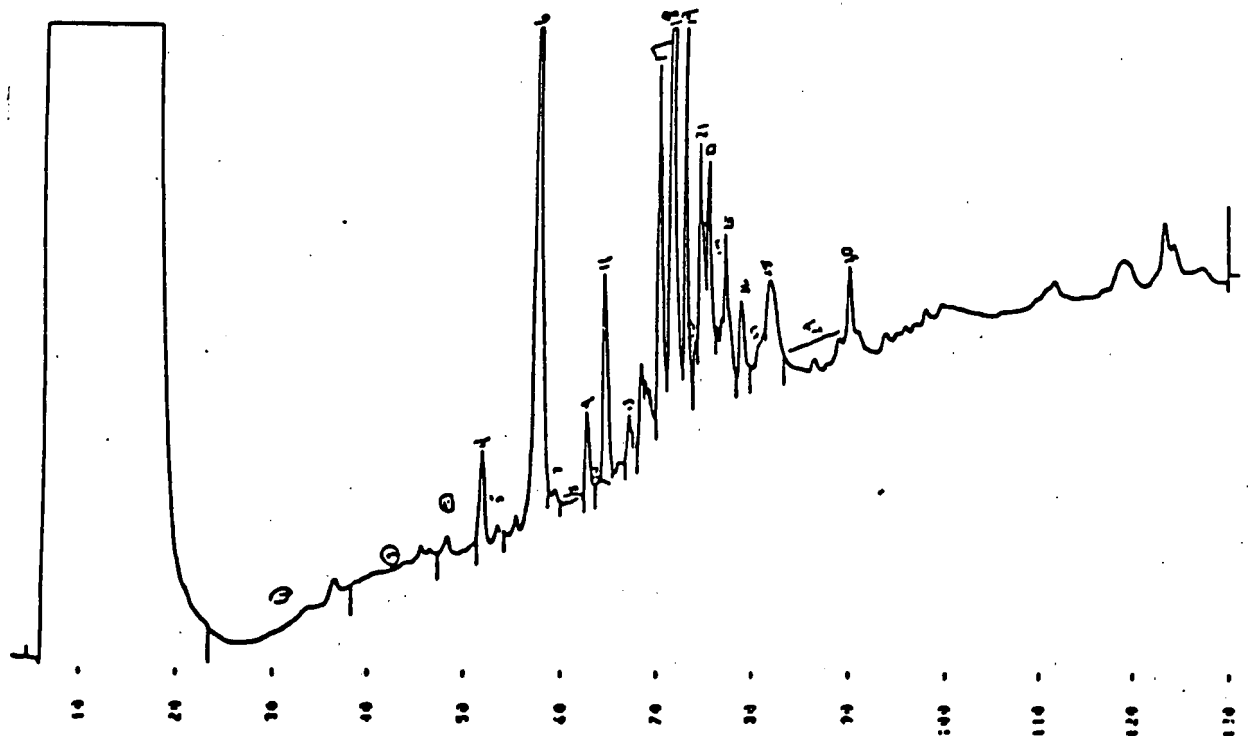
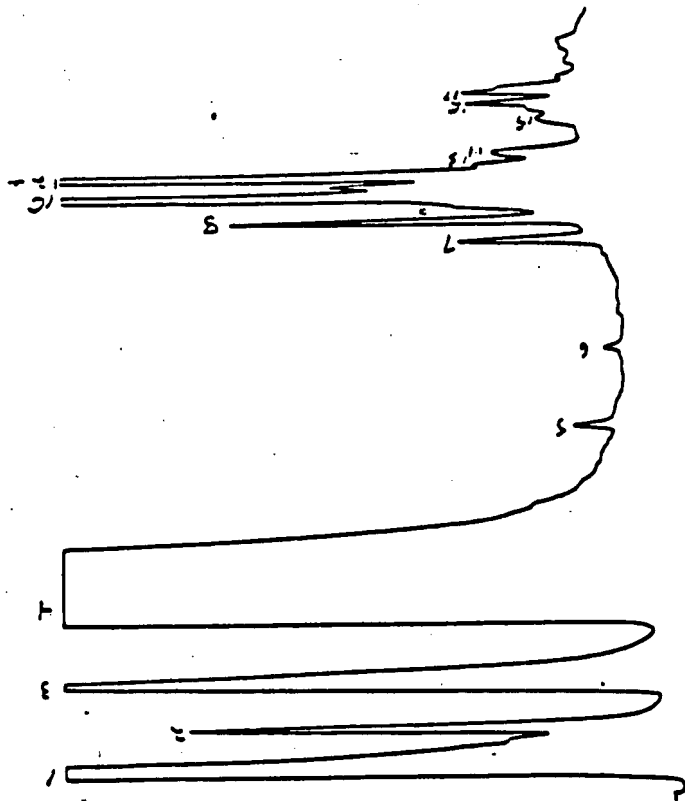
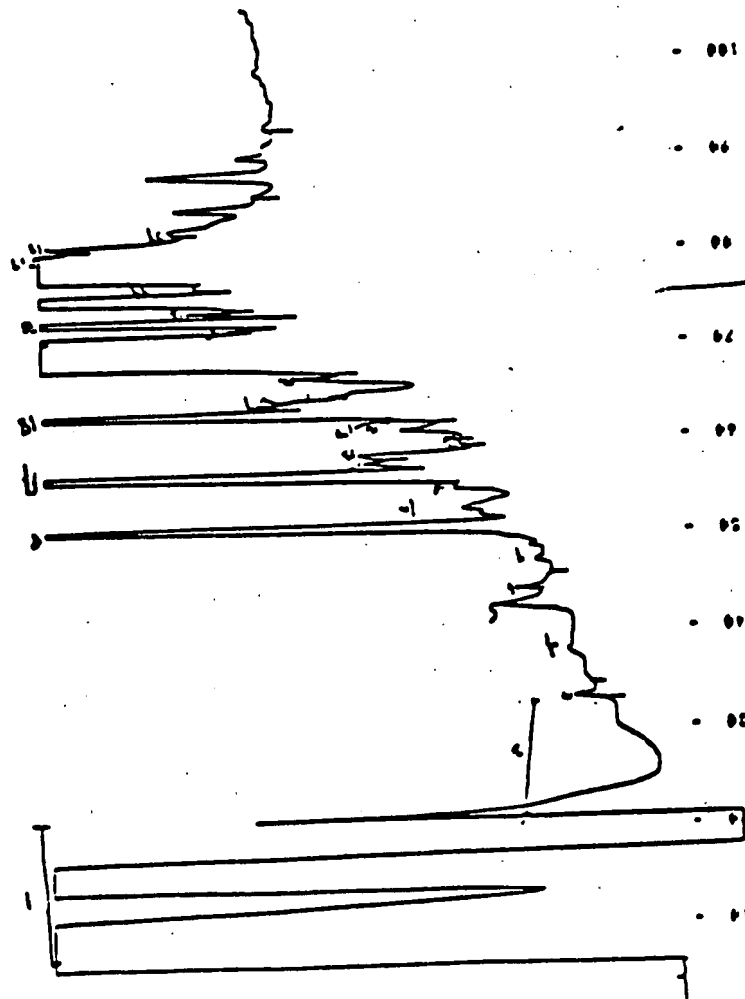


FIG 9B: ALKYLATED

* Lys-C digests of
TNF-BP

re-chromatograph
evens # 24, 26, 28, 32, 34



100
80
60
40
20
0

9

10

11

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12

13

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98

99

100

re-chromatograph
odds # 13, 15, 17, 33, 37

100
80
60
40
20
0

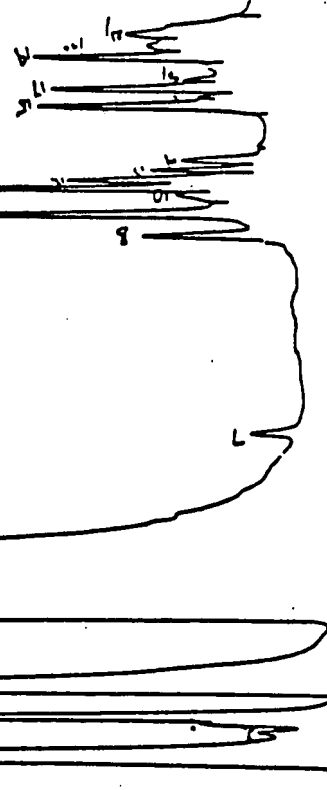
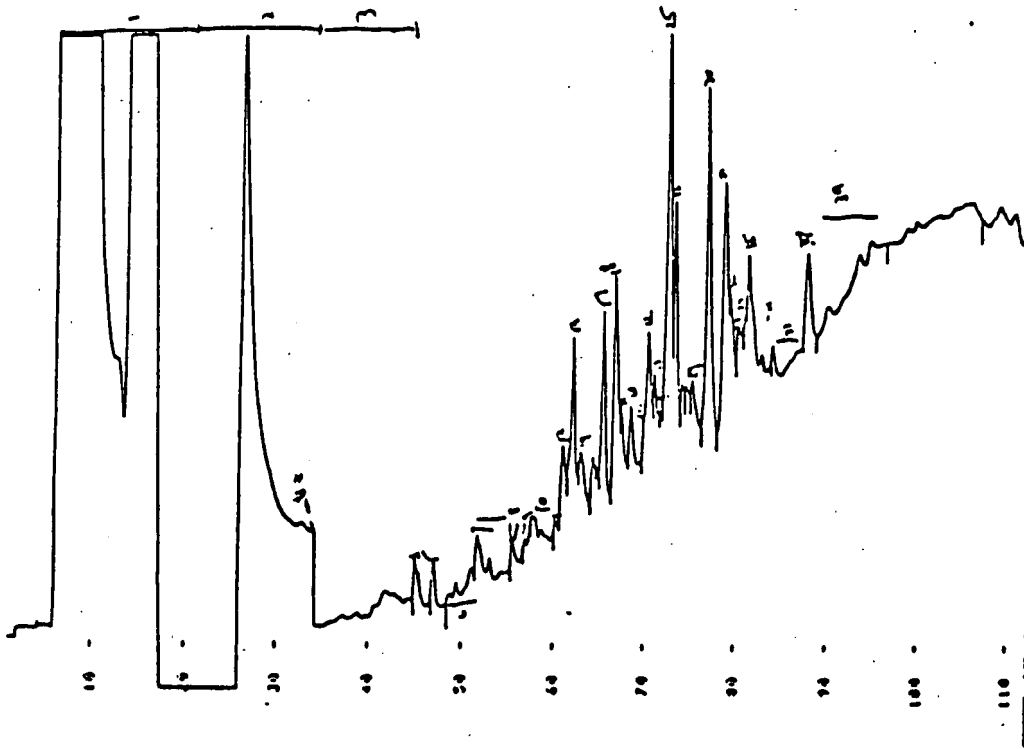


FIG. 10

#1



#2

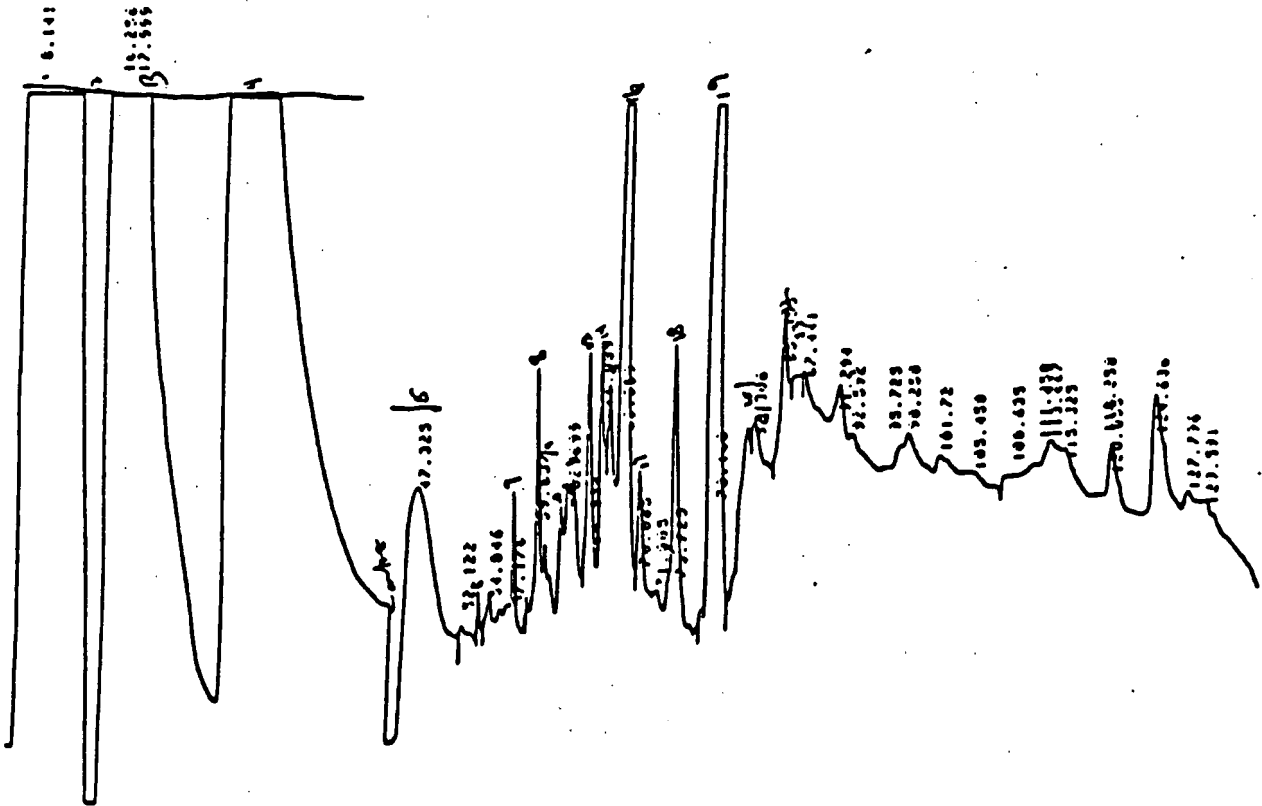
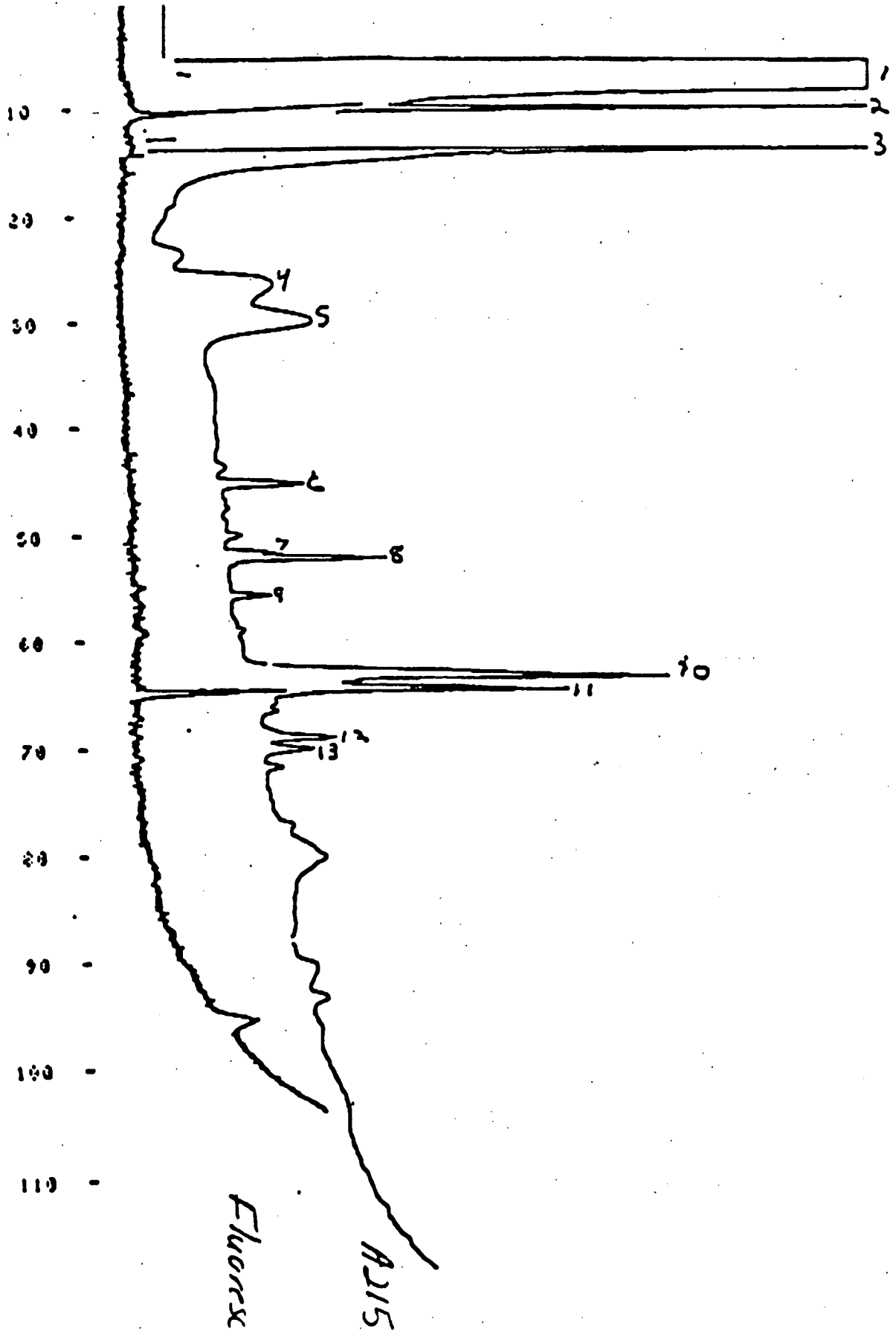


FIG. 11A



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Fig. 11B

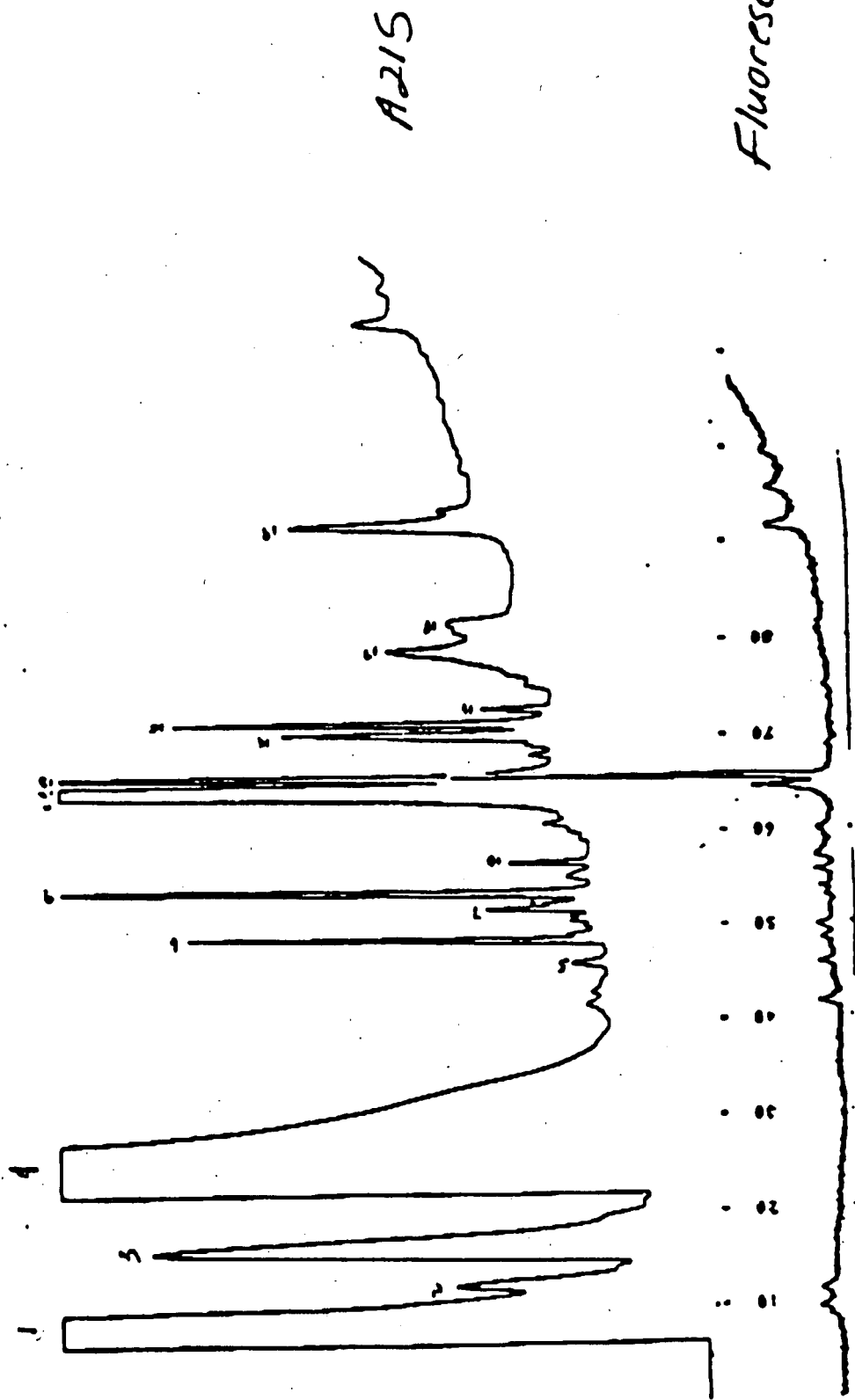


Figure 12

A. 1 10 20 30 40 50 60
 DSVCPQCKYIPQNH SICCTKCKHKGITLYHOCPPGQDTC - - - SCSFTASEHRLRLCLSCS - - - K -
 B. (E) ZOWTVCTCHAGFLRENECVSC(L)HC(K)(E)(C)(L)(K)(E)
 C. (K) ENEGOVEISSCTVDRTVCCCKE(C)(V)(R)(H)(Y) - (O)
 (O)
 (K)(S)LECTKLCCLPOTEN - (S)(H)P(S)(A)
 (O)(A)

10 20 30 40 50 60 70
 CATGCTGCA GGTGACTCT AGAGGATCTG GGUCCTACTA GCTTTGAGTT GAGGGAACAA AAATGAALAC

80 90 100 110 120 130 140
 ACAGGACAAAC TAGAGAACA TTAAGCATCA GATTGTATGC CCCAACTGTC TAAGTTTCAG GGAAGAAGTC

150 160 170 180 190 200 210
 TAAACTTAGT GAGTGGCCTG GCCTGGGCGG AATGTTTCAC TGAGGAAGGA CTGGAUCCAG GGAAGTTTAA

220 230 240 250 260 270 280
 GATCTGCTAC CCCTAAGCTT CCCATCCCTC CCTCTCTTGA TGGTGTCTCC TCTATCTGAT TCTTCCCCAG

289 298 307 316 325 334
 GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCG TCA GGG GTT ATT GGA CTG GTC
 Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly Leu Val

343 352 361 370 379 388
 CCT CAC CTA GGG GAC AGG GAG AAG AGA GAT AGT GTG TGT CCC CAA GCA AAA TAT
 Pro His Leu Gly Asp Arg Glu Lys Arg Asp Ser Val Cys Pro Gln Gly Lys Tyr

397 406 415 424 433 444
 ATC CAC CCT CAA AAT AAT TCG ATT TGC TGT ACC AAG TGC CAC AAA G GTAGGGGCAA
 Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys Ala

454 464 474 484 494 504 514
 GTGGAAACGG TGAATGCCCT CAGGTCTGGG GTGCTGCTTC TTTCTCTGCT TCTTCCAGTT GTTCTTCCCT

524 534 544 554 564 574 584
 AACTTTGCTG TCTCTCTGG GUTGGGATT TCTCCCTCCC TCCTCTCCTA GAGACTTCAQ GGAATCGGCC

594 604 614 624 634 644 654
 CTGGCTGTTG TCCTAGCAT GGGGCTCCTT CCTTGTGTTT TCACCCGCAG CCTAACTCTG CGGCCCCATT

664 673 682 691 700
 CA CA GGA ACC TAC TTG TAC AAT GAC TGT CCA GGC CCG GGG CAG GAT ACC GAC
 Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp

709 718 727 736 745 754
 TGC AGG GAG TGT GAG AGC GGC TCC TTC ACC GCT TCA GAA AAC CAC CTC AAG CAC
 Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu Arg His

763 772 781 797 807 817
 TGC CTC AGC TGC TCC AAA TGC CCA AAG GGTGAGTGT CACAGGCAGG AGAGTCAGGC
 Cys Leu Ser Cys Ser Lys Cys Arg Lys

827 837 847 857 867 877 887
 GGGTCTTGAQ TGGTGTGTGG GTGCCTGTCT ATGTGCAGGC TGGTGGGTOT GGGCAGGAAG GTGTGTGTTT

897 907 917 927 937 947 957
 TGTGCTGACA CTGATGGAT GTGAGTGTGT ATTACAGAGA CACACACTTA GGGGTATGTC AGHAAGGUXA

967 977 987 997 1007 1016
 TGCAGGAGAA GGAUGAIGCA GAACTCATAC CCCATCTTCT CCCCACCA GAA ATG GAT CAG
 Glu Met Gly Gln

1025
 GTG GAG ATC
 Val Glu Ile

FIG. 14

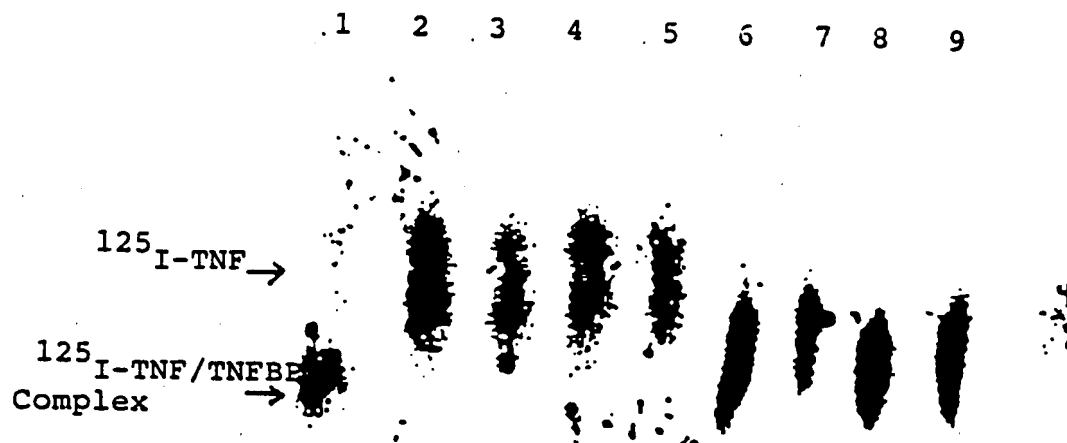
1 10 20 30 40 50 60 70 80
DSVCPQCKYINPOMNSICCTKCNKGTLYNDPCPCGQDTDCRECESGSFTASENNLRNCLSCSKCKCKEMGQVEISSCTVORDT

90
VCGCRKN

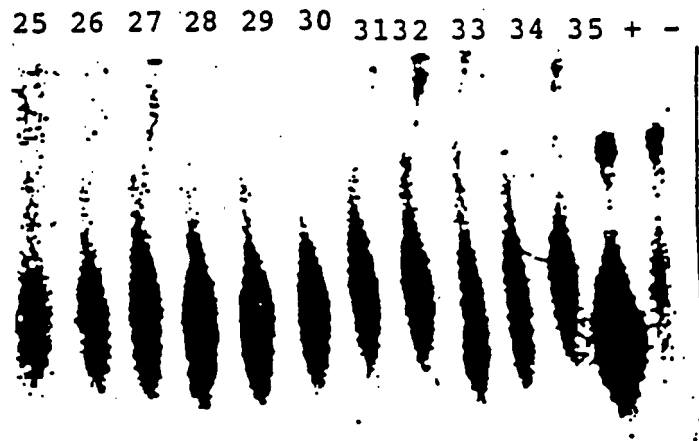
KONTVCTCHAGFFLRENECVSC

LECTKLCLPOIEN

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Lane 1 is a positive control. Purified TNF-BP complexed with $^{125}\text{I-TNF}$. Lane 2-5 are protein from the 24, 48, 72, and 96 hour incubations with PMA/PHA that did not bind to the TNF-affinity column. Lane 6-9 are the material from the same incubations that did bind to the TNF-affinity column.



Fractions 27, 28 and 29, 33 and 34 show TNF binding activity. + is as lane 1 of figure 15. - is ^{125}I -TNF alone.

NO	PMA/PHA	
PMA/PHA	1hr	17hr

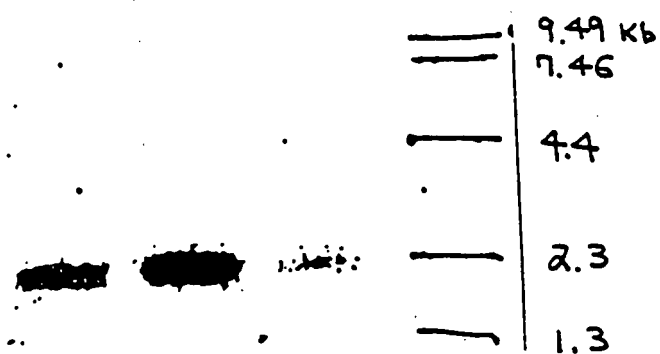


Fig 17



FIG 18

10
 Asp Ser Val Cys Pro Gln Gly Lys Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr 20
 30
 Lys Cys His Lys Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp 40
 50
 Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu Arg His Cys Leu 60
 70
 Ser Cys Ser Lys Cys Arg Lys Glu Met Gly Gln Val Glu Ile Ser Ser Cys Thr Val Asp 80
 90
 Arg Asp Thr Val Cys Gly Cys Arg Lys Asn Gln Tyr Arg His Tyr Trp Ser Glu Asn Leu 100
 110
 Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu Asn Gly Thr Val His Leu Ser Cys Gln Glu 120
 130
 Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Phe Phe Leu Arg Glu Asn Glu Cys Val 140
 150
 Ser Cys Ser Asn Cys Lys Lys Ser Leu Glu Cys Thr Lys Leu Cys Leu Pro Gln Ile Glu 160
 161
 Asn

FIG 19

296			305		
<u>GAT</u>	<u>AGT</u>	<u>GTG</u>	<u>TGT</u>	<u>CCC</u>	<u>CAG</u>
Asp	Ser	Val	Cys	Pro	Gln

314				323				332				341				350				359			
GGA	AAA	TAT	ATC	CAC	CCT	CAA	AAT	AAT	TCG	ATT	TGC	TGT	ACC	AAG	TGC	CAC	AAA						
Gly	Lys	Tyr	Ile	His	Pro	Gln	Asn	Asn	Ser	Ile	Cys	Cys	Thr	Lys	Cys	His	Lys						
368				377				386				395				404				413			
GGA	ACC	TAC	TTG	TAC	AAT	GAC	TGT	CCA	GGC	CCG	GGG	CAG	GAT	ACG	GAC	TGC	AGG						
Gly	Thr	Tyr	Leu	Tyr	Asn	Asp	Cys	Pro	Gly	Pro	Gly	Gln	Asp	Thr	Asp	Cys	Arg						
422				431				440				449				458				467			
GAG	TGT	GAG	AGC	GGC	TCC	TTC	ACC	GCT	TCA	GAA	AAC	CAC	CTC	AGA	CAC	TGC	CTC						
Glu	Cys	Glu	Ser	Gly	Ser	Phe	Thr	Ala	Ser	Glu	Asn	His	Leu	Arg	His	Cys	Leu						
476				485				494				503				512				521			
AGC	TGC	TCC	AAA	TGC	CGA	AAG	GAA	ATG	GGT	CAG	GTG	GAG	ATC	TCT	TCT	TGC	ACA						
Ser	Cys	Ser	Lys	Cys	Arg	Lys	Glu	MET	Gly	Gln	Val	Glu	Ile	Ser	Ser	Cys	Thr						
530				539				548				557				566				575			
GTG	GAC	CGG	GAC	ACC	GTG	TGT	GGC	TGC	AGG	AAG	AAC	CAG	TAC	CGG	CAT	TAT	TGG						
Val	Asp	Arg	Asp	Thr	Val	Cys	Gly	Cys	Arg	Lys	Asn	Gln	Tyr	Arg	His	Tyr	Trp						
584				593				602				611				620				629			
AGT	GAA	AAC	CTT	TTC	CAG	TGC	TTC	AAT	TGC	AGC	CTC	TGC	CTC	AAT	GGG	ACC	GTG						
Ser	Glu	Asn	Leu	Phe	Gln	Cys	Phe	Asn	Cys	Ser	Leu	Cys	Leu	Asn	Gly	Thr	Val						
638				647				656				665				674				683			
CAC	CTC	TCC	TGC	CAG	GAG	AAA	CAG	AAC	ACC	GTG	TGC	ACC	TGC	CAT	GCA	GGT	TTC						
His	Leu	Ser	Cys	Gln	Glu	Lys	Gln	Asn	Thr	Val	Cys	Thr	Cys	His	Ala	Gly	Phe						
692				701				710				719				728				737			
TTT	CTA	AGA	GAA	AAC	GAG	TGT	GTC	TCC	TGT	AGT	AAC	TGT	AAG	AAA	AGC	CTG	GAG						
Phe	Leu	Arg	Glu	Asn	Glu	Cys	Val	Ser	Cys	Ser	Asn	Cys	Lys	Lys	Ser	Leu	Glu						
746				755				764															
TGC	ACG	AAG	TTG	TGC	CTA	CCC	CAG	ATT	GAG	AAT													
Cys	Thr	Lys	Leu	Cys	Leu	Pro	Gln	Ile	Glu	Asn													

Figure 20.

10 20 30 40 50 60 70
 SATCACTGGG ACCAGGCCGT GATCTCTATG CCCGAGTCTC AACCTCAAC TGTCACCCCA AGGCACTTGG

80 90 100 110 120 130 140
 GACGTCCTGG ACAGACCGAG TCCCGGGAAG CCCGAGCACT GCCGCTGCCA CACTGCCCTG AGCCCAAATG

150 160 171 180 189 198
 GGGGAGTGAG AGGCCATAGC TGTCTGGC
 ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG
 MET Gly Leu Ser Thr Val Pro Asp Leu Leu

207 216 225 234 243 252
 CTG CCG CTG GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT
 Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile

261 270 279 288 297 306
 GGA CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA GAT AGT GTG TGT CCC CAA
 Gly Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg Asp Ser Val Cys Pro Gln

315 324 333 342 351 360
 GGA AAA TAT ATC CAC CCT CAA AAT AAT TCG ATT TGC TGT ACC AAG TGC CAC AAA
 Gly Lys Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys

369 378 387 396 405 414
 GGA ACC TAC TTG TAC AAT GAC TGT CCA GGC CCG GGG CAG GAT ACG GAC TGC AGG
 Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp Cys Arg

423 432 441 450 459 468
 GAG TGT GAG AGC GGC TCC TTC ACC GCT TCA GAA AAC CAC CTC AGA CAC TGC CTC
 Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu Arg His Cys Leu

477 486 495 504 513 522
 AGC TGC TCC AAA TGC CGA AAG GAA ATG GGT CAG GTG GAG ATC TCT TCT TGC ACA
 Ser Cys Ser Lys Cys Arg Lys Glu MET Gly Gln Val Glu Ile Ser Ser Cys Thr

531 540 549 558 567 576
 GTG GAC CGG GAC ACC GTG TGT GGC TGC AGG AAG AAC CAG TAC CGG CAT TAT TGG
 Val Asp Arg Asp Thr Val Cys Gly Cys Arg Lys Asn Gln Tyr Arg His Tyr Trp

585 594 603 612 621 630
 AGT GAA AAC CTT TTC CAG TGC TTC AAT TGC AGC CTC TGC CTC AAT GGG ACC GTG
 Ser Glu Asn Leu Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu Asn Gly Thr Val

639 648 657 666 675 684
 CAC CTC TCC TGC CAG GAG AAA CAG AAC ACC GTG TGC ACC TGC CAT GCA GGT TTC
 His Leu Ser Cys Gln Glu Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Phe

Fig 21

693			702			711			720			729			738		
TTT	CTA	AGA	GAA	AAC	GAG	TGT	GTC	TCC	TGT	AGT	AAC	TGT	AAG	AAA	AGC	CTG	GAG
Phe	Leu	Arg	Glu	Asn	Glu	Cys	Val	Ser	Cys	Ser	Asn	Cys	Lys	Lys	Ser	Leu	Glu
747			756			765			774			783			792		
TGC	ACG	AAG	TTG	TGC	CTA	CCC	CAG	ATT	GAG	AAT	GTT	AAG	GGC	ACT	GAG	GAC	TCA
Cys	Thr	Lys	Leu	Cys	Leu	Pro	Gln	Ile	Glu	Asn	Val	Lys	Gly	Thr	Glu	Asp	Ser
801			810			819			828			837			846		
GGC	ACC	ACA	GTG	CTG	TTG	CCC	CTG	GTC	ATT	TTC	TTT	GGT	CTT	TGC	CTT	TTA	TCC
Gly	Thr	Thr	Val	Leu	Leu	Pro	Leu	Val	Ile	Phe	Phe	Gly	Leu	Cys	Leu	Leu	Ser
855			864			873			882			891			900		
CTC	CTC	TTC	ATT	GGT	TTA	ATG	TAT	CGC	TAC	CAA	CGG	TGG	AAG	TCC	AAG	CTC	TAC
Leu	Leu	Phe	Ile	Gly	Leu	MET	Tyr	Arg	Tyr	Gln	Arg	Trp	Lys	Ser	Lys	Leu	Tyr
909			918			927			936			945			954		
TCC	ATT	GTT	TGT	GGG	AAA	TGG	ACA	CCT	GAA	AAA	GAG	GGG	GAG	CTT	GAA	GGG	ACT
Ser	Ile	Val	Cys	Gly	Lys	Ser	Thr	Pro	Glu	Lys	Glu	Gly	Glu	Leu	Glu	Gly	Thr
963			972			981			990			999			1008		
ACT	ACT	AAG	CCC	CTG	GCC	CCA	AAC	CCA	AGC	TTC	AGT	CCC	ACT	CCA	GGC	TTC	ACC
Thr	Thr	Lys	Pro	Leu	Ala	Pro	Asn	Pro	Ser	Phe	Ser	Pro	Thr	Pro	Gly	Phe	Thr
1017			1026			1035			1044			1053			1062		
CCC	ACC	CTG	GGC	TTC	AGT	CCC	GTC	CCC	AGT	TCC	ACC	TTC	ACC	TCC	AGC	TCC	ACC
Pro	Thr	Leu	Gly	Phe	Ser	Pro	Val	Pro	Ser	Ser	Thr	Phe	Thr	Ser	Ser	Ser	Thr
1071			1080			1089			1098			1107			1116		
TAT	ACC	CCC	GGT	GAC	TGT	CCC	AAC	TTT	GCG	GCT	CCC	CGC	AGA	GAG	GTG	GCA	CCA
Tyr	Thr	Pro	Gly	Asp	Cys	Pro	Asn	Phe	Ala	Ala	Pro	Arg	Arg	Glu	Val	Ala	Pro
1125			1134			1143			1152			1161			1170		
CCC	TAT	CAG	GGG	GCT	GAC	CCC	ATC	CTT	GCG	ACA	GCC	CTC	GCC	TCC	GAC	CCC	ATC
Pro	Tyr	Gln	Gly	Ala	Asp	Pro	Ile	Leu	Ala	Thr	Ala	Leu	Ala	Ser	Asp	Pro	Ile
1179			1188			1197			1206			1215			1224		
CCC	AAC	CCC	CTT	CAG	AAG	TGG	GAG	GAC	AGC	GCC	CAC	AAG	CCA	CAG	AGC	CTA	GAC
Pro	Asn	Pro	Leu	Gln	Lys	Trp	Glu	Asp	Ser	Ala	His	Lys	Pro	Gln	Ser	Leu	Asp
1233			1242			1251			1260			1269			1278		
ACT	GAT	GAC	CCC	GCG	ACG	CTG	TAC	GCC	GTG	GTG	GAG	AAC	GTG	CCC	CCG	TTG	CGC
Thr	Asp	Asp	Pro	Ala	Thr	Leu	Tyr	Ala	Val	Val	Glu	Asn	Val	Pro	Pro	Leu	Arg
1287			1296			1305			1314			1323			1332		
TGG	AAG	GAA	TTC	GTG	CGG	CGC	CTA	GGG	CTG	AGC	GAC	CAC	GAG	ATC	GAT	CGG	CTG
Trp	Lys	Glu	Phe	Val	Arg	Arg	Leu	Gly	Leu	Ser	Asp	His	Glu	Ile	Asp	Arg	Leu

1341

1350

1359

1368

1377

1386

GAG CTG CAG AAC GGG CGC TGC CTG CGC GAG GCG CAA TAC AGC ATG CTG GCG ACC
 Glu Leu Gln Asn Gly Arg Cys Leu Arg Glu Ala Gln Tyr Ser MET Leu Ala Thr

1395

1404

1413

1422

1431

1440

TGG AGG CCG CGC ACG CCG CGG CGC GAG GCC ACG CTG GAG CTG CTG GGA CCG GTG
 Trp Arg Arg Arg Thr Pro Arg Arg Glu Ala Thr Leu Glu Leu Leu Gly Arg Val

1449

1458

1467

1476

1485

1494

CTC CGC GAC ATG GAC CTG CTG GGC TGC CTG GAG GAC ATC GAG GAG GCG CTT TGC
 Leu Arg Asp MET Asp Leu Leu Gly Cys Leu Glu Asp Ile Glu Glu Ala Leu Cys

1503

1512

1521

1530

1546

1556

GGC CCC GCC GCC CTC CCG CCC GCG CCC AGT CTT CTC AGA TGA GGCTGCGCCC CTGCGGGCAG
 Gly Pro Ala Ala Leu Pro Pro Ala Pro Ser Leu Leu Arg

1566

1576

1586

1596

1606

1616

1626

CTCTAAGBAC CGTCCTGCGA GATCGCCTTC CAACCCCACT TTTTCTGGA AAGGAGGGGT CCTGCAGGGG

1636

1646

1656

1666

1676

1686

1696

CAAGCAGGAG CTAGCAGCCG CCTACTTGGT GCTAACCCTT CGATGTACAT AGCTTTTCTC AGCTGCCTGC

1706

1716

1726

1736

1746

1756

1766

GCGCCGCCGA CAGTCAGCGC TGTGCGCGCG GAGAGAGGTG CGCCGTGGGC TCAAGAGCCT GAGTGGGTGG

1776

1786

1796

1806

1816

1826

1836

TTTGCAGGGA TGAGGGACGC TATGCCTCAT GCCCGTTTTG GGTGTCCTCA CCAGCAAGGC TGCTCGGGGG

1846

1856

1866

1876

1886

1896

1906

CCCCTGGTTC GTCCCTGAGC CTTTTTCACA GTGCATAAGC AGTTTTTTTT GTTTTTGTTT TGTGTTGTTT

1916

1926

1936

1946

1956

1966

1976

TGTTTTTAAA TCAATCATGT TACACTAATA GAAACTTGGC ACTCCTGTGC CCTCTGCCTG GACAAGCACA

1986

1996

2006

2016

2026

2036

2046

TAGCAAGCTG AACTGTCCTA AGGCAGGGGC GAGCACGGAA CAATGGGGCC TTCAGCTGGA GCTGTGGACT

2056

2066

2076

2086

TTTGTACATA CACTAAAATT CTGAAGTTAA AGCTCAAAAA AA

FIG. 22

GA ATT CCA CAA CGG TTT CCC TCT AGA AAT AAT TTT GTT TAA CTT TAA GAA GGA GAT ATA CAT

Start gene 10 protein sequence

ATG GCT AGC ATG ACT GGT GGA CAG CAA ATG GGT ACG GAT CCG ATC TTG GAG GAT GAT TAA
Met Ala Ser Met Thr Gly Gly Gln Met Gly Thr Asp Pro Ile Leu Glu Asp Asp Stop
Translational coupler

ATG GAC AGC GTT TGC CCC
Met Asp Ser Val Cys Pro
Start TNF inhibitor Sequence

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Fig. 23

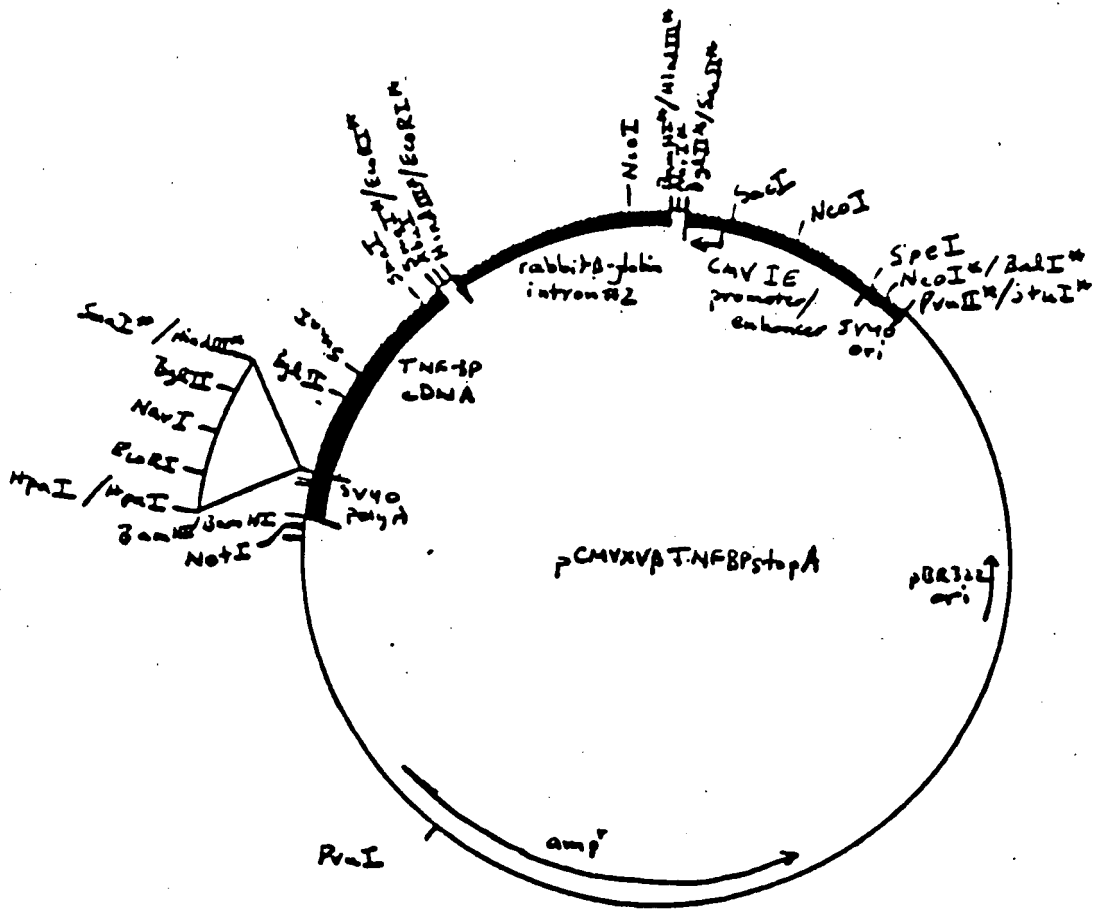
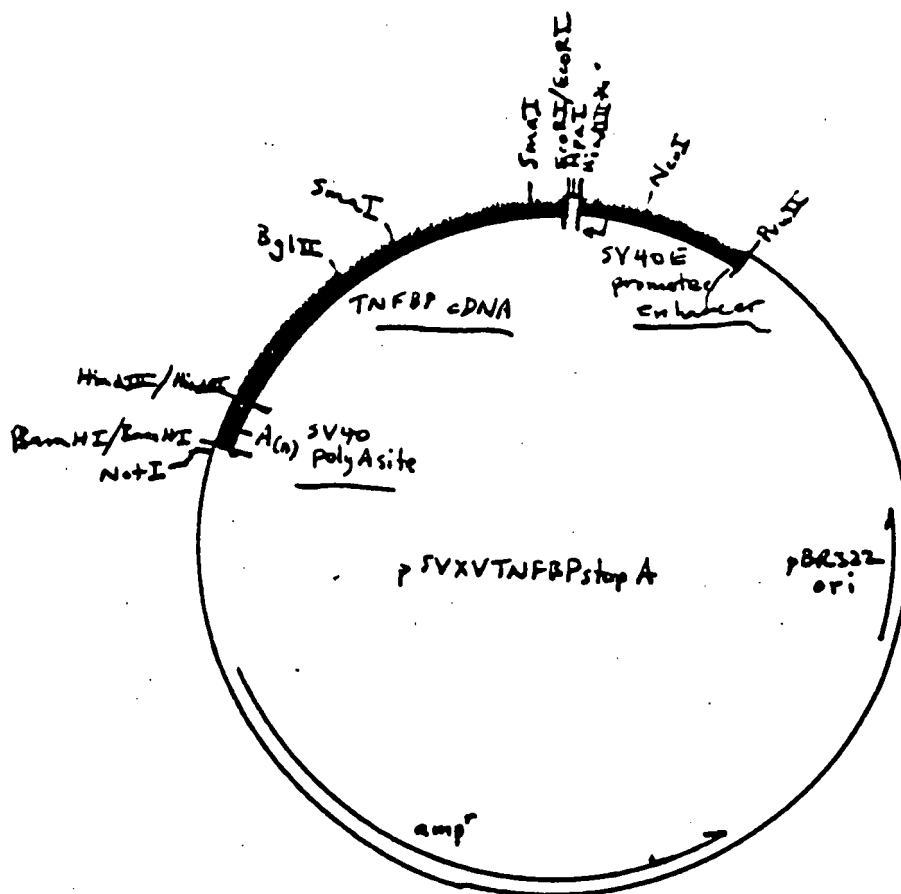


Fig. 24

08/484337



* - restriction site no longer exists.

173/4
68
Aug.
20

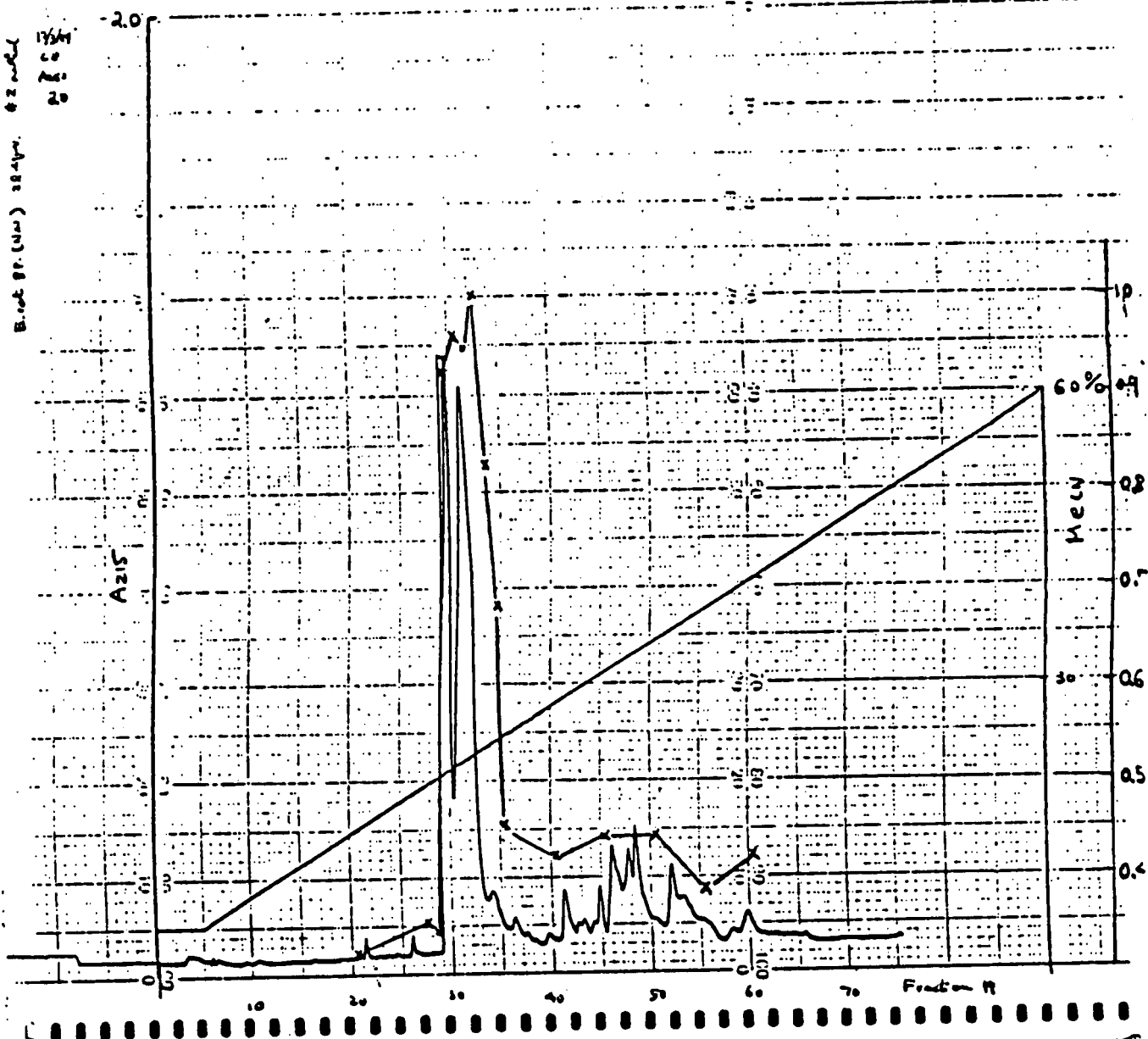


Figure 25

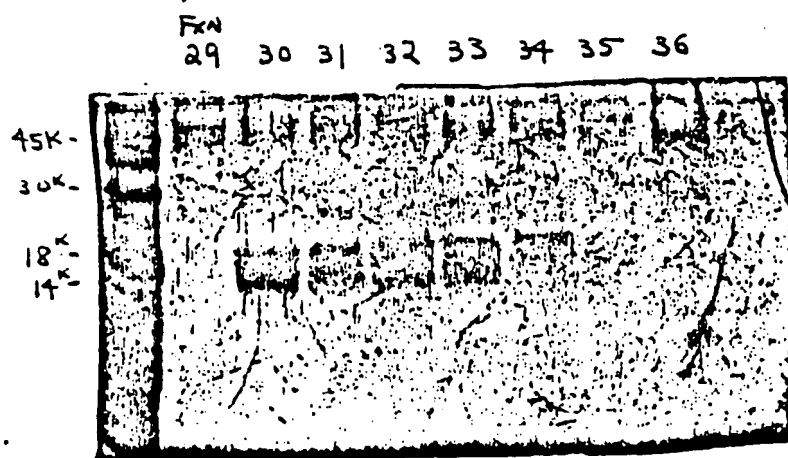


Figure 26

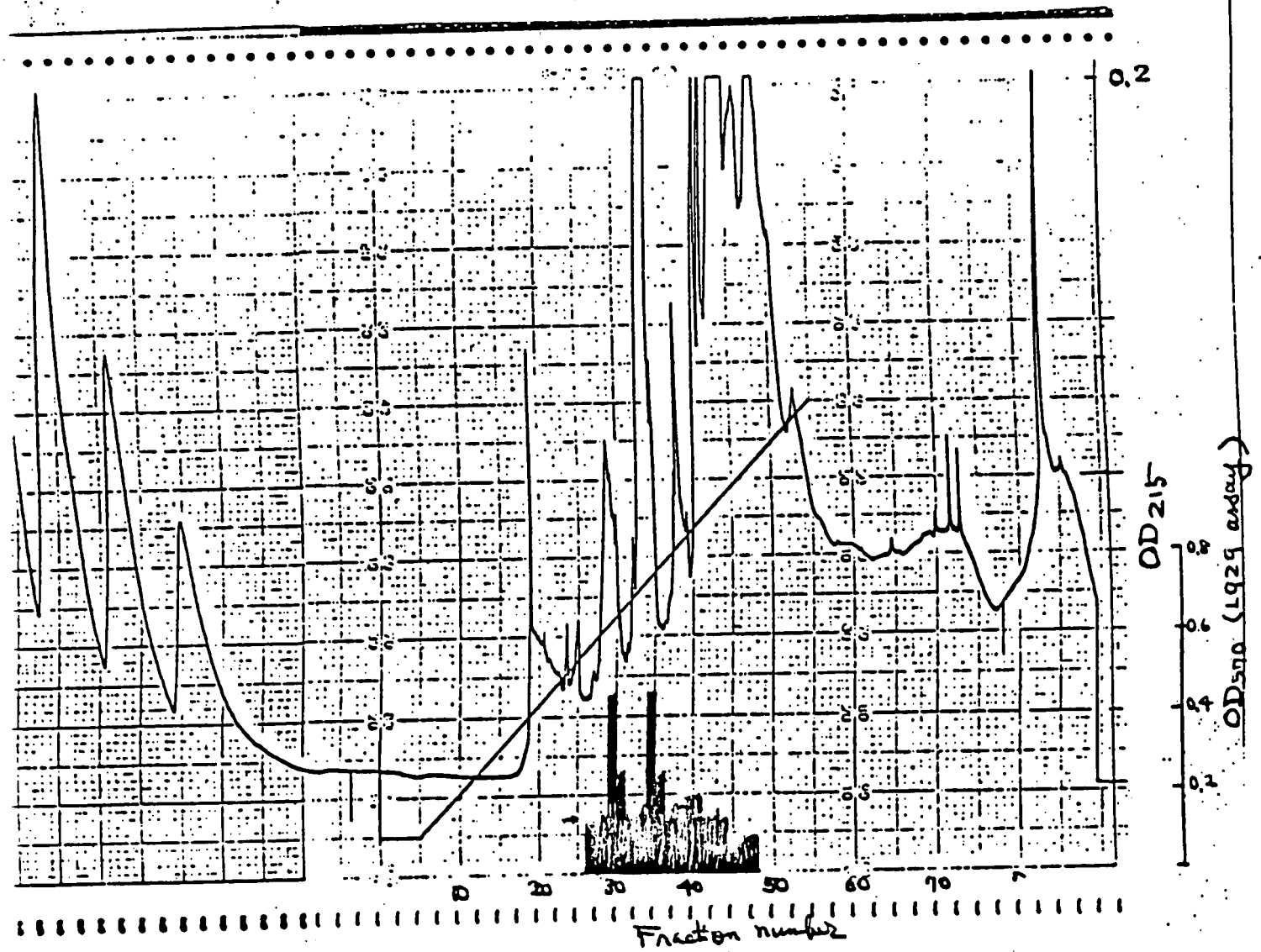
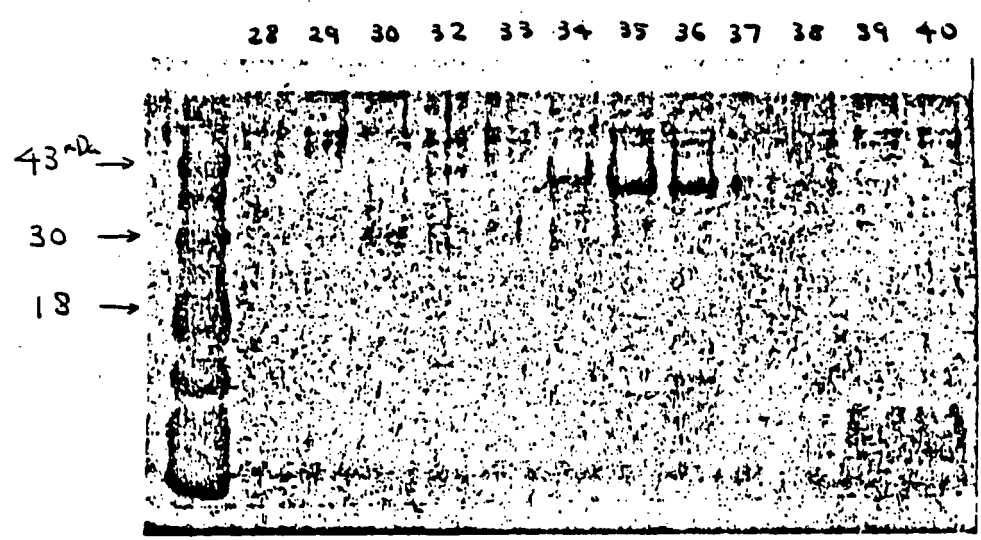


Fig. 27



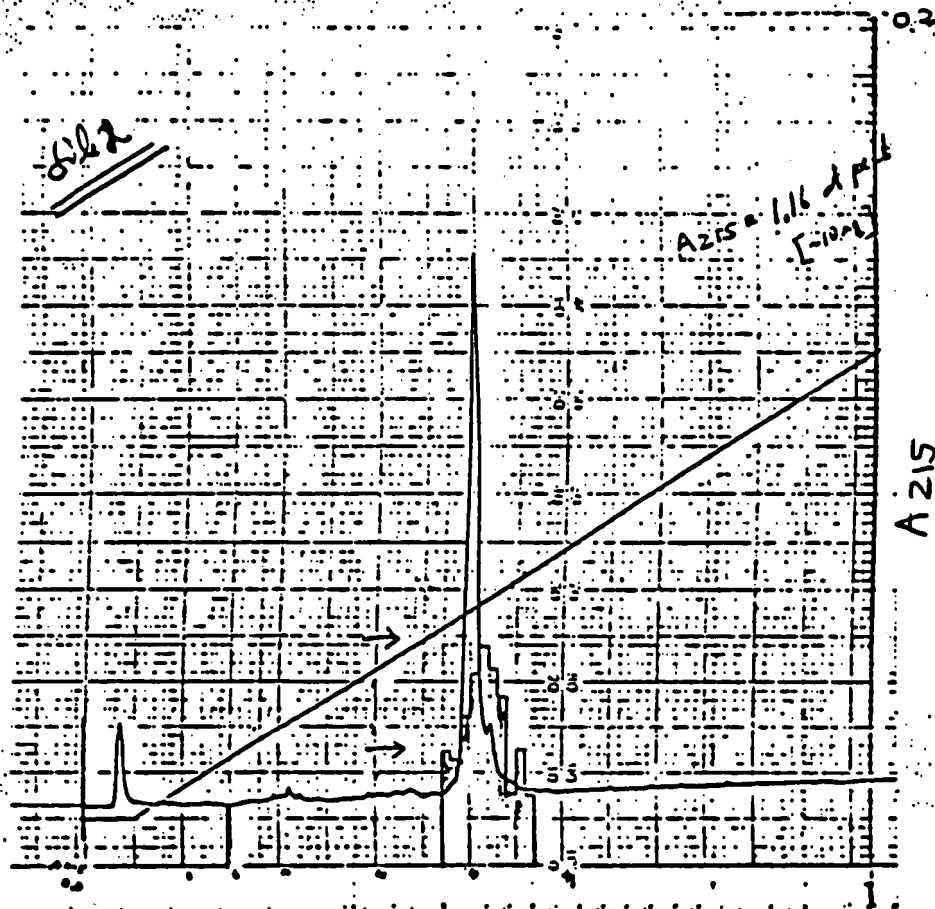
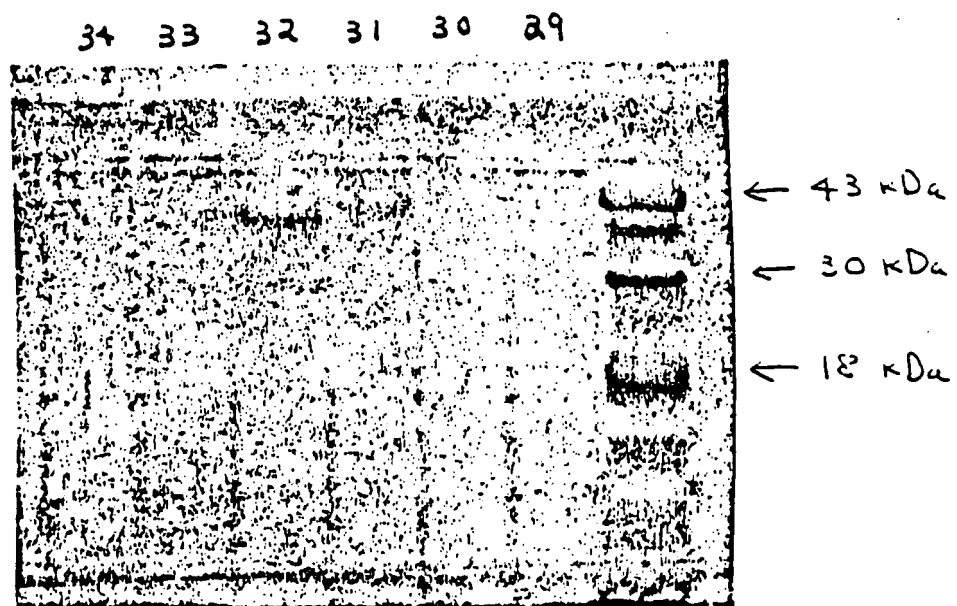


Fig. 29



U937-derived TNF-INH1 (30 kDa)

()-()-Val-()-Pro-Gln-GLY-Lys-Tyr-Ile-His-Pro-Gln-
()-Asn-()-Ile

U939-derived TNF-INH2 (40 kDa)

Leu-Pro-Ala-Gln-Val-Ala-Phe-Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-
Ser-Thr-Cys-Arg-Leu-Arg-Glu-Tyr-Tyr-Asp-Gln-Thr-Ala-Gln-Met-
Cys-Cys-Ser-Lys-Cys-

Urine-derived TNF-INH2 (40 kDa)

Ala-Gln-Val-Ala-Phe-Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr-
Cys-()-Leu-()-Glu

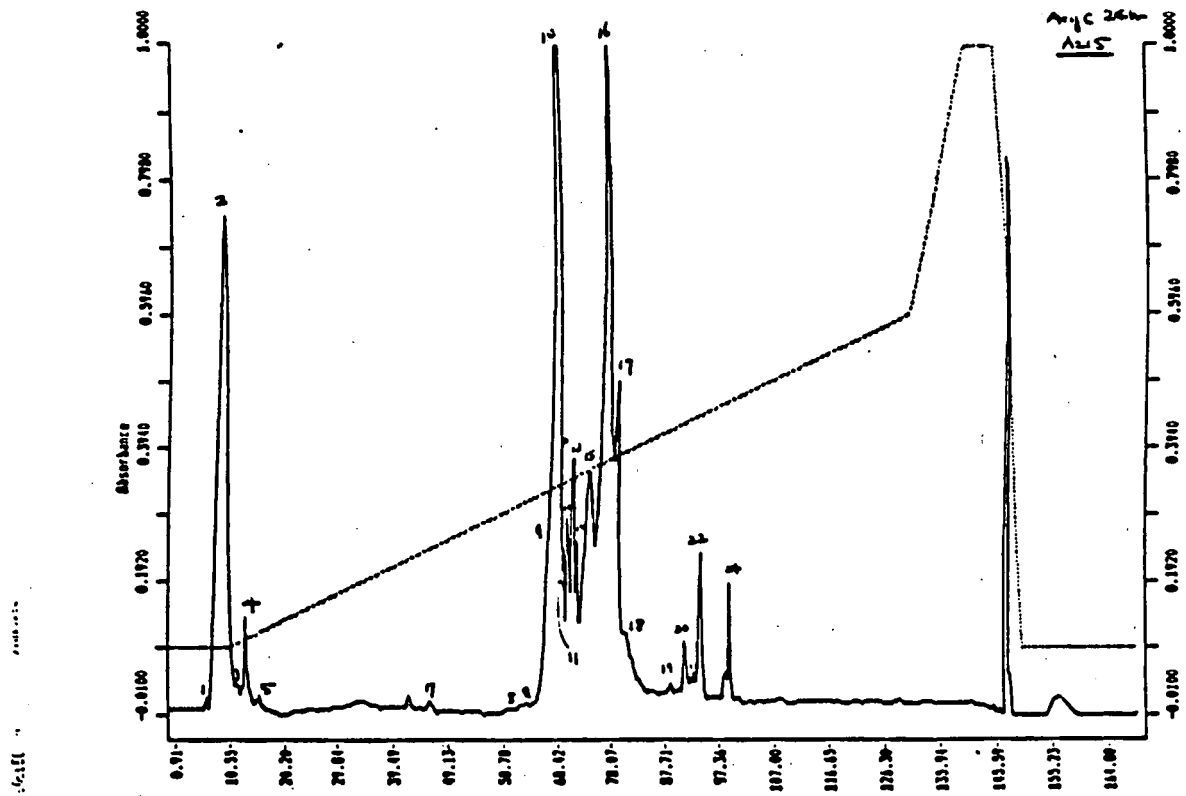


Figure 33

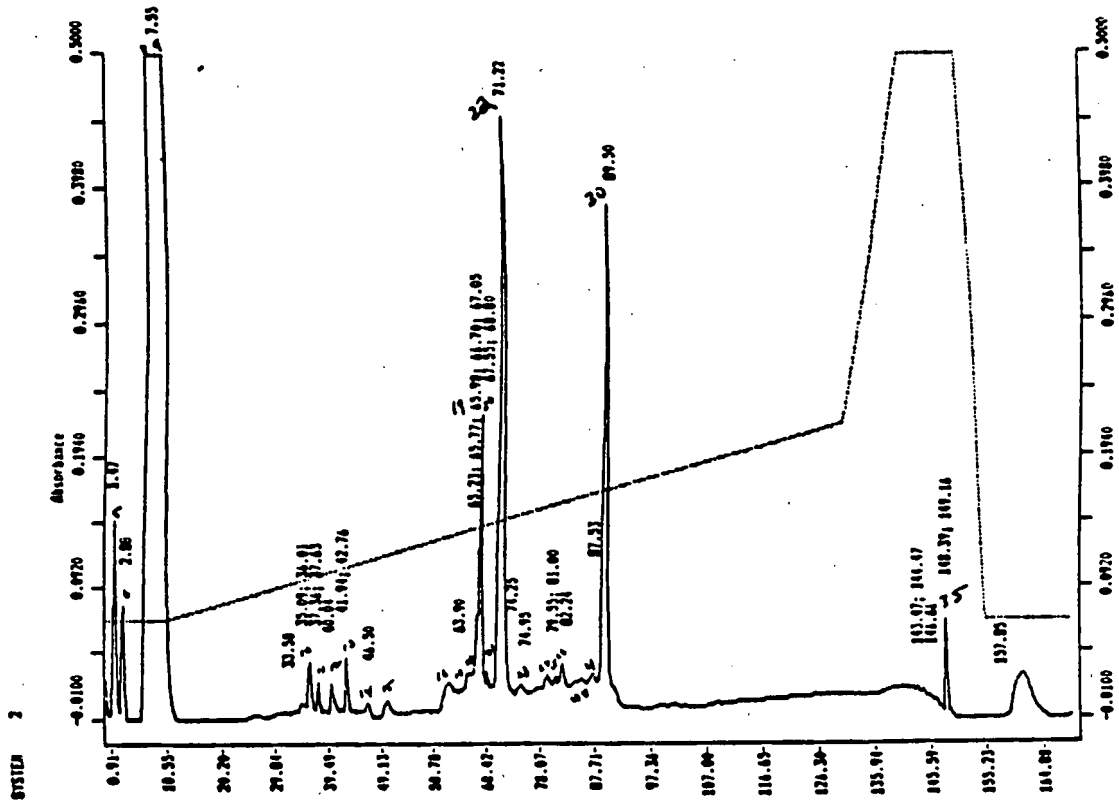


Figure 34

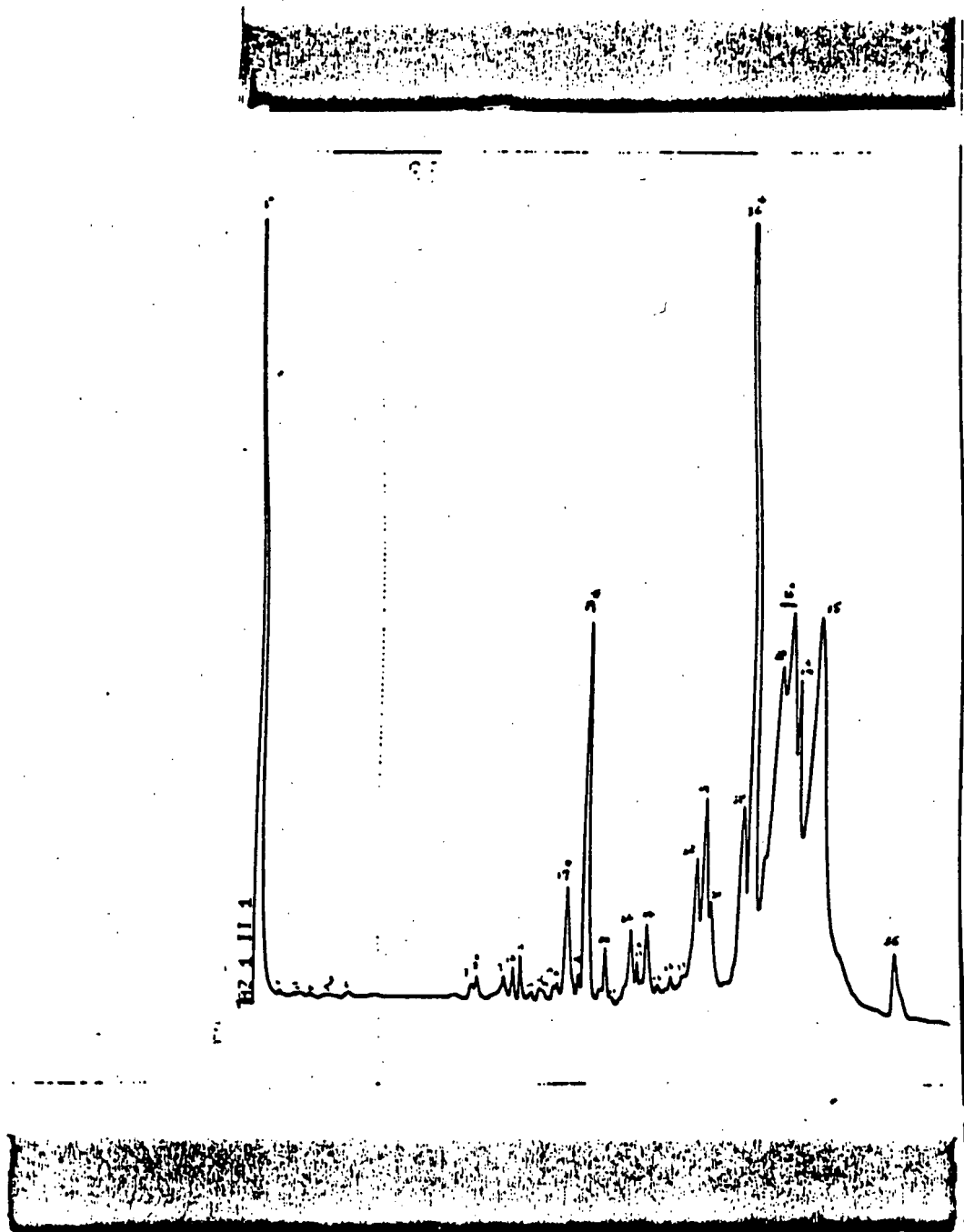


Figure 35

1 10 20 30 40 50 60 70 80
I P A Q V A F T P V A P E P G S T C R L R E V Y D O T A Q H C C S K C S P G Q H A K V F C T K T S O T V C D S C E D S T Y T Q L _ N _ V P E C L S C G S R C S S

NT

V25 V34.35

V37 V6

R12 R16

R4

R16 T30

R16 T30 V9 R16 T30 V4

R4

90 100 110 120 130 140 150
O Q V E _ _ A C T R E Q H R I C T C R P G W Y C A L S K Q E C R L C A P L R K C R P G F G V A R P G T E T S D V V C K P C A P G T F S _ T T S (T J D) (P) (C) (R) (P)

V23 V20

R4 R14 R10

R16 T13

R10 C19 R10 C32 R10 C17

R10

08/484337

Figure 37

5' - CCG
Fro

53			64			73			82			91			100		
<u>GAG</u> Glu	<u>CCC</u> Pro	<u>GCG</u> Gly	<u>AGC</u> Ser	<u>ACA</u> Thr	<u>TGC</u> Cys	<u>CGG</u> Arg	<u>CTC</u> Leu	<u>AGA</u> Arg	<u>GAA</u> Glu	<u>TAC</u> Tyr	<u>TAT</u> Tyr	<u>GAC</u> Asp	<u>CAG</u> Gln	<u>ACR</u> Thr	<u>GCW</u> Ala	<u>CAH</u> Gln	<u>ATG</u> MET
105			118			127			136			145			154		
<u>TGC</u> Cys	<u>TGC</u> Cys	<u>AGC</u> Ser	<u>AAG</u> Lys	<u>TGC</u> Cys	<u>TGG</u> Ser	<u>CCG</u> Pro	<u>GGC</u> Gly	<u>CAA</u> Gln	<u>CAT</u> His	<u>GCA</u> Ala	<u>AAA</u> Lys	<u>GTC</u> Val	<u>TTC</u> Phe	<u>TGT</u> Cys	<u>ACC</u> Thr	<u>AAG</u> Lys	<u>ACC</u> Thr
163			172			181			190			199			208		
<u>TGG</u> Ser	<u>GAC</u> Asp	<u>ACC</u> Thr	<u>GTG</u> Val	<u>TGT</u> Cys	<u>GAC</u> Asp	<u>TCC</u> Ser	<u>TGT</u> Cys	<u>GAG</u> Glu	<u>GAC</u> Asp	<u>AGC</u> Ser	<u>ACA</u> Thr	<u>TAC</u> Tyr	<u>ACC</u> Thr	<u>CAG</u> Gln	<u>CTC</u> Leu	<u>TGG</u> Trp	<u>AAC</u> Asn
217			226			235			244			253			262		
<u>TGG</u> Trp	<u>GTT</u> Val	<u>CCC</u> Pro	<u>GAG</u> Glu	<u>TGC</u> Cys	<u>TTG</u> Leu	<u>AGC</u> Ser	<u>TGT</u> Cys	<u>GGC</u> Gly	<u>TCC</u> Ser	<u>CGC</u> Arg	<u>TGT</u> Cys	<u>AGC</u> Ser	<u>TCT</u> Ser	<u>GAC</u> Asp	<u>CAG</u> Gln	<u>GTG</u> Val	<u>GAA</u> Glu
271			280			289			298			307			316		
<u>ACT</u> Thr	<u>CAA</u> Gln	<u>GCC</u> Ala	<u>TGC</u> Cys	<u>ACT</u> Thr	<u>CGG</u> Arg	<u>GAA</u> Glu	<u>CAG</u> Gln	<u>AAC</u> Asn	<u>CGC</u> Arg	<u>ATC</u> Ile	<u>TGC</u> Cys	<u>ACC</u> Thr	<u>TGC</u> Cys	<u>AGG</u> Arg	<u>CCC</u> Pro	<u>GGC</u> Gly	<u>TGG</u> Trp

325

TAY TGC - 3'
Tyr Cys

Figure 38

Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser
Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln MET Cys Cys
Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr
Ser Asp Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu
Trp Asn Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser
Asp Gln Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys
Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys
Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala
Arg Pro Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro
Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr Asp Ile Cys Arg Pro His
Gln Ile Cys Asn Val Val Ala Ile Pro Gly Asn Ala Ser Arg Asp Ala
Val Cys Thr Ser Thr Ser Pro Thr Arg Ser MET Ala Pro Gly Ala Val
His Leu Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr Gln Pro Thr
Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro MET Gly
Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly Asp

10 30 40 50 70
 DAATTCGGCG CAGCGG TGGAGAGAG GCGCTGGCT GCGAGGCGC GAGGGGGA GGGCAGGGGG

60	70	101	110	119
CAACCGGACC	CCGCCCGCAC	CC ATG GCG CCC GTC GCG GTC TGG GCG GCG CTG GCC		
		MET Ala Pro Val Ala Val Trp Ala Ala Leu Ala		
128	137	146	155	164
GTC GGA CTG GAG CTC TGG GCT GCG GCG CAC GCG TTG CCC GCG CAG GTG GCA TTT				
Val Gly Leu Glu Leu Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe				
182	191	200	209	218
ACA CCC TAC GCG CCG GAG CCC GGG AGC ACA TGC CCG CTC AGA GAA TAC TAT GAC				
Thr Pro Tyr Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp				
236	245	254	263	272
CAG ACA GCT CAG ATG TGC TGC AGC AAG TGC TCG CCG GCG CAA CAT GCA AAA GTC				
Gln Thr Ala MET Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val				
290	299	308	317	326
TTC TGT ACC AAG ACC TCG GAC ACC GTG TGT GAC TCC TGT GAG GAC AGC ACA TAC				
Phe Cys Thr Lys Thr Ser Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr				
344	353	362	371	380
ACC CAG CTC TGG AAC TGG GTT CCC GAG TGC TTG AGC TGT GCG TCC CCG TGT AGC				
Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser				
398	407	416	425	434
TCT GAC CAG GTG GAA ACT CAA GCC TGC ACT CCG GAA CAG AAC CCG ATC TGC ACC				
Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys Thr				
452	461	470	479	488
TGC AGC CCC GCG TGG TAC TGC GCG CTG AUC AAG CAG GAG GGG TGC CCG CTG TGC				
Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys Arg Leu Cys				
506	515	524	533	542
GCG CCG CTG CCG AAG TGC CCG CCG GCG TTC GCG GTG GCG AGA CCA GGA ACT GAA				
Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu				
560	569	578	587	596
ACA TCA GAC GTG GTG TGC AAG CCC TGT GCC CCG GGG ACG TTC TCC AAC ACG ACT				
Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr				
614	623	632	641	650
TCA TCC ACG GAT ATT TGC AAG CCC CAC CAG ATC TGT AAC GTG GTG GCG ATC CCT				
Ser Ser Thr Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro				
668	677	686	695	704
GGG AAT GCA AGC AGG GAT GCA GTC TGC ACG TCC ACG TCC CCC ACC CCG AGT ATG				
Gly Asn Ala Ser Arg Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser MET				
722	731	740	749	758
GCC CCA GGG GCA GTA CAC TTA CCC CAG CCA GTG TCC ACA CCA TCC CAA CAC ACG				
Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr				
776	785	794	803	812
CAG CCA ACT CCA GAA CCC AGC ACT GCT CCA AGC ACC TCC TTC CTG CTC CCA ATG				
Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro MET				
830	839	848	857	866
GGC CCC AGC CCC CCA GCT GAA GGG AGC ACT GCG GAC TTC GCT CTT CCA GTT GGA				
Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly Asp Phe Ala Leu Pro Val Gly				
884	893	902	911	920
CTG ATT GTG GGT GTG ACA GCC TTG GGT CTA CTA ATA ATA GGA GTG GTG AAC TGT				
Leu Ile Val Gly Val Thr Ala Leu Gly Leu Leu Ile Ile Gly Val Val Asn Cys				
938	947	956	965	974
GTC ATC ATG ACC CAG GTG AAA AAG AAG CCC TTG TGC CTC CAG AGA GAA GCC AAG				
Val Ile MET Thr Gln Val Lys Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys				
992	1001	1010	1019	1028
GTG CCT CAC TTG CCT GCG GAT AAG GCG CCG GGT ACA CAG AGC CCC GAG CAG CAG				
Val Pro His Leu Pro Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln				

Figure
39

1044 1059 1064 1073 1082
CAC CTG CTG ATC ACA GCG CCG AGC TCC AGC AGC AGC TCC CTG GAG AGC TCG GCC
His Leu Leu Ile Thr Ala Pro Ser Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala

1100 1109 1118 1127 1136 1145
AGT GCG TTG GAC AGA AGG GCG CCC ACT CCG AAC CAG CCA CAG GCA CCA GCG GTG
Ser Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly Val

1154 1163 1172 1181 1190 1199
GAG GCC AGT GGG GCG GGG GAG GCG CCG GCG AGC ACC GGG AGC TCA GAT TCT TCC
Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser Asp Ser Ser

1208 1217 1226 1235 1244 1253
CCT GGT GGC CAT GGG ACC CAG GTC AAT GTC ACC TGC ATC GTG AAC GTC TGT AGC
Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile Val Asn Val Cys Ser

1262 1271 1280 1289 1298 1307
AGC TCT GAC CAC AGC TCA CAG TGC TCC TCC CAA GCC AGC TCC ACA ATG GGA GAC
Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln Ala Ser Ser Thr MET Gly Asp

1316 1325 1334 1343 1352 1361
ACA GAT TCC AGC CCC TCG GAG TCC CCG AAG GAC GAG CAG GTC CCC TTC TCC AAG
Thr Asp Ser Ser Pro Ser Glu Ser Pro Lys Asp Glu Gln Val Pro Phe Ser Lys

1370 1379 1388 1397 1406 1415
GAG GAA TGT GCG TTT CCG TCA CAG CTG GAG ACC CCA GAG ACC CTG CTG GGA AGC
Glu Glu Cys Ala Phe Arg Ser Gln Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser

1424 1433 1442 1451 1460 1469
ACC GAA GAG AAG CCC CTG CCC CTT GGA GTG CCT GAT GCT GAG ATG AAG CCC AGT
Thr Glu Glu Lys Pro Leu Pro Leu Gly Val Pro Asp Ala Gly MET Lys Pro Ser

1478 1488 1498 1508 1518 1528 1538
TAA CCAGGCCGGT GTGGGCTGTG TCGTAGCCAA GGTGGGCTGA GCCCTGGCAG GATGACCCTG

1548 1558 1568 1578 1588 1598 1608
CGAAGGCGCC CTGCTCTTC CAGGCCCCCA CCACTAGGAC TCTGAGGCTC TTCTGAGCC AAGTTCTCT

1618 1628 1638 1648 1658 1668 1678
AGTGCCTCC ACAGCCGCA GCTCCTCTG ACCTGCAGGC CAAGAGCAGA GGCAGCGGT TGTGAAAGC

1688 1698 1708 1718 1728 1738 1748
CTCTGCTCC ATGGTGTGTC CCTCTCGAA GGTGCTGTC GCATGGACGT TCAGGCGATG CTGGGCAAG

1758 1768 1778 1788 1798 1806 1818
TCCCTUACTC TCTGTGACCT GCGCCGCCCA GCTGCACCTG CCAGCCTGCG TTCTGAGCC CTTGGTTTT

1828 1838 1848 1858 1868 1878 1888
TTGTTTGTGTT GTTGTGTTGT TTGTTTGTGTT CTCGCCCTGG GCTCTGCCCC AGCTCTGGCT TCCAGAAAAC

1898 1908 1918 1928 1938 1948 1958
CCCAGCATCC TTTCTGCAG AGGCGCTTTC TGGAGAGGAG GGATGCTGCC TGAGTCACCC ATGAGAGAG

1968 1978 1988 1998 2008 2018 2028
GACAGTGCTT CAGCCTGAGG CTGAGACTGC GGGATGCTCC TGGGCTCTG TGCAGGAGG AGGTGGCAGC

2038 2048 2058 2068 2078 2088 2098
CCTGTAGGGA ACAGGCTCCT TCAAGTTAGC TCAGGAGGCT TGGAAAGCAT CACCTCAGGC CACTGTGCCC

2108 2118 2128 2138 2148 2158 2168
ACCCGATTT AACTCTTTT TCTCCCAAT GGGATATAG GACCTGTCC TTTGTATCAG AAAAGGAGAT

2178 2188 2198 2208 2218
TGTGAGCAAG AGGCAATTA ATAATATGG CCAATATTT AAAAAACCG AATTC

Figure
39 cont.

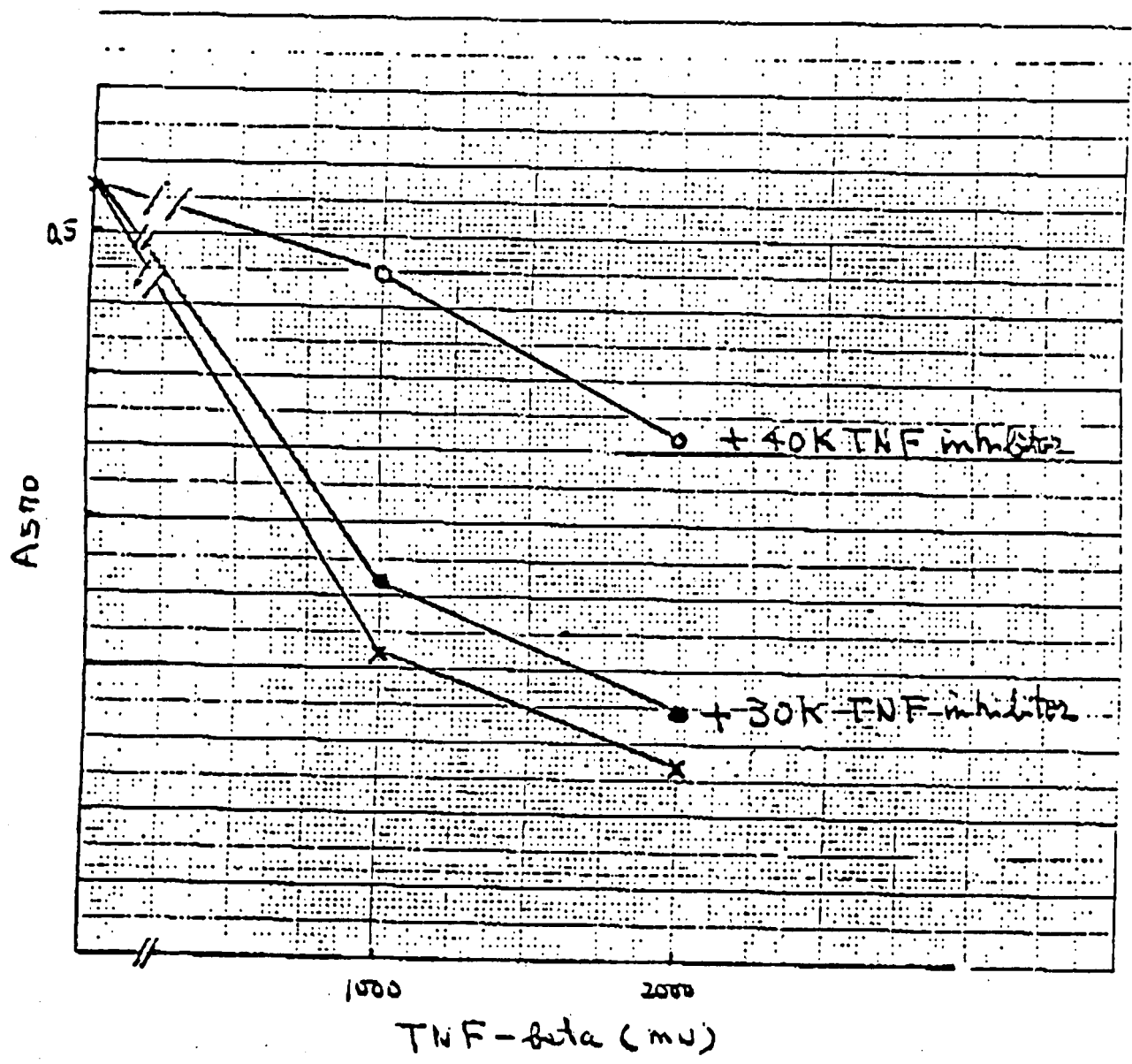


Figure 40

Figure 41

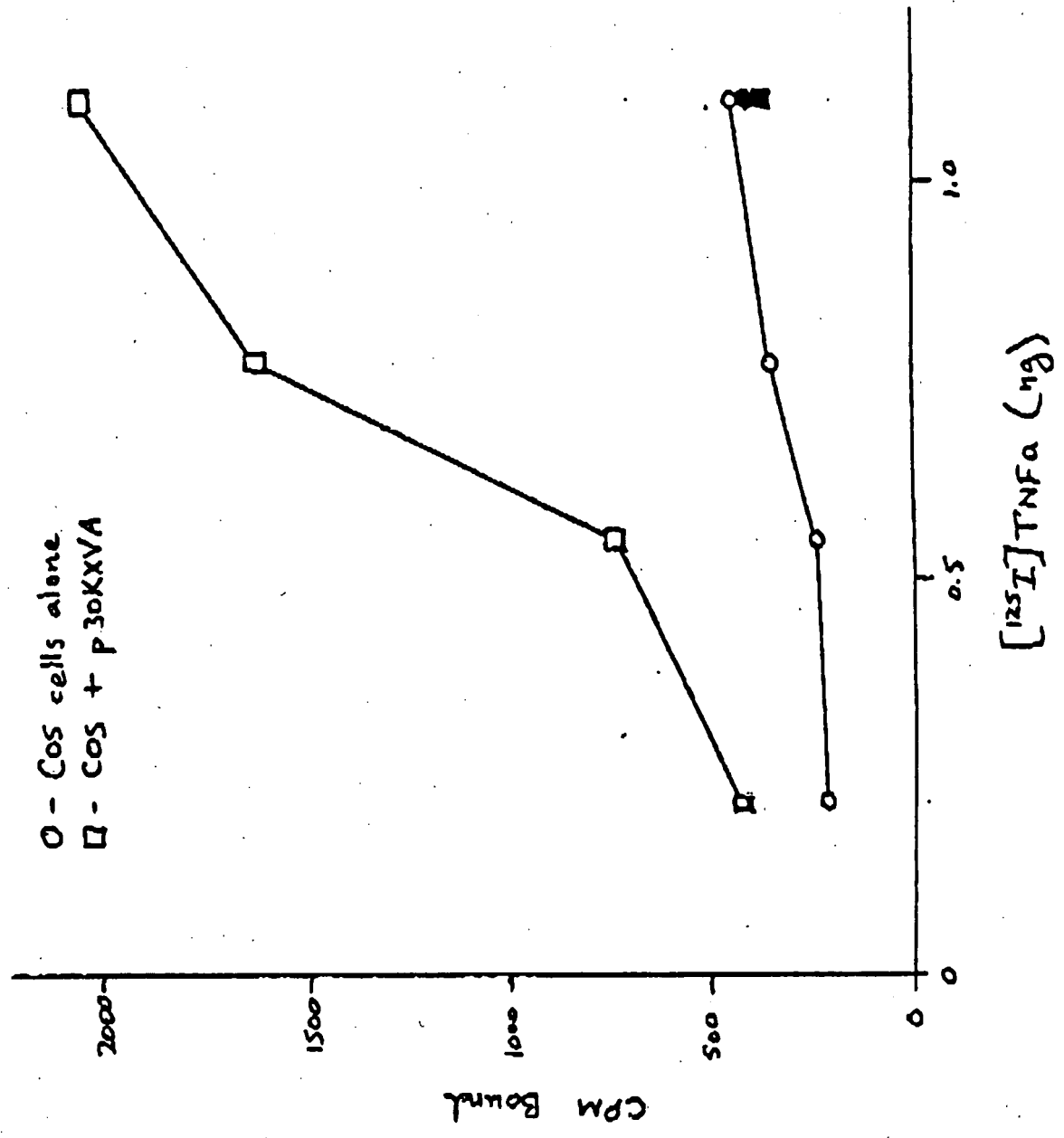
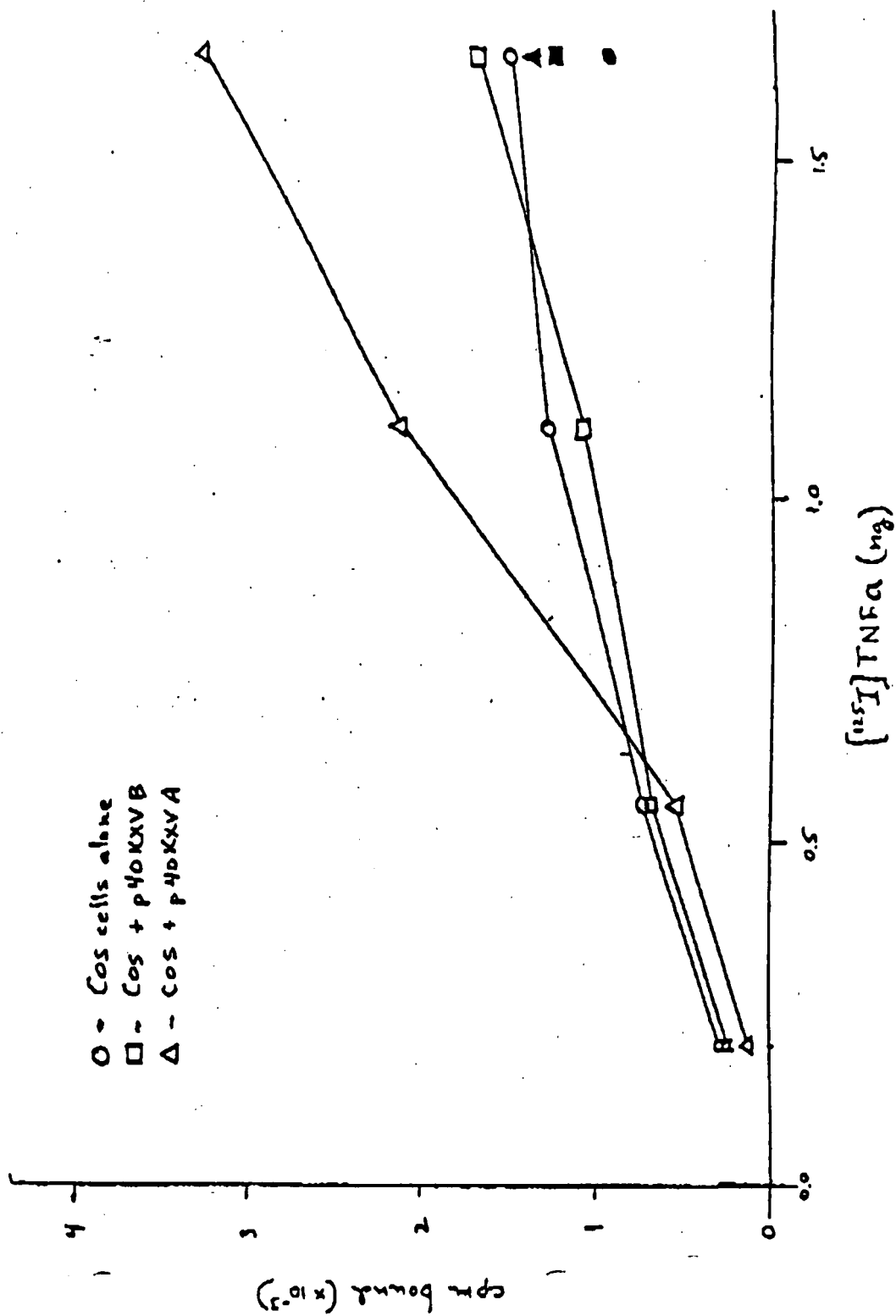


Figure 42



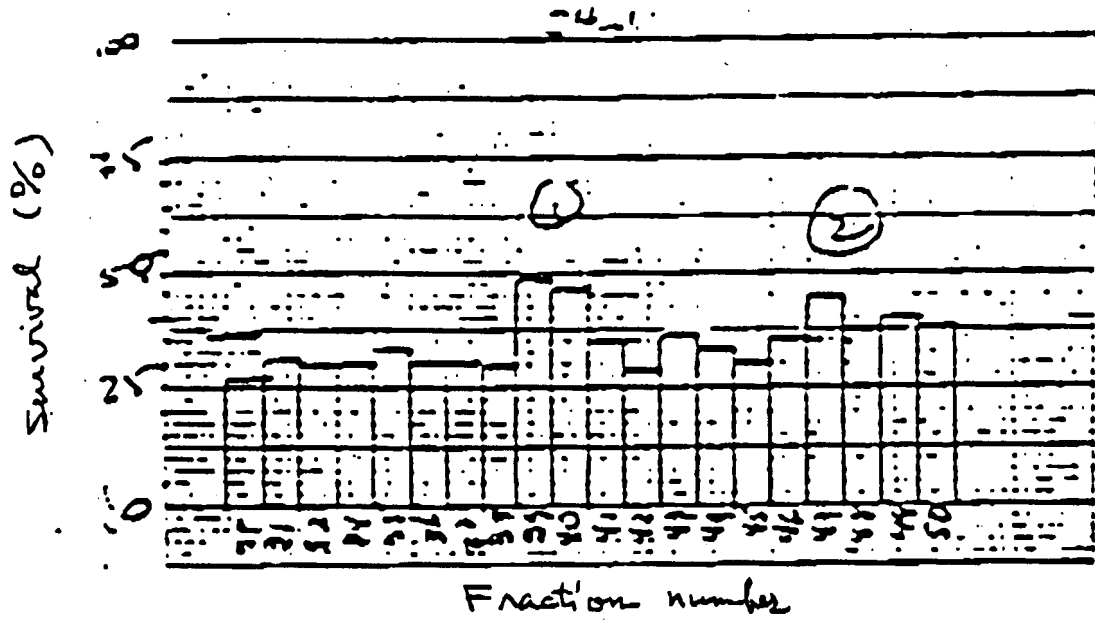


FIG 43

FIG 44

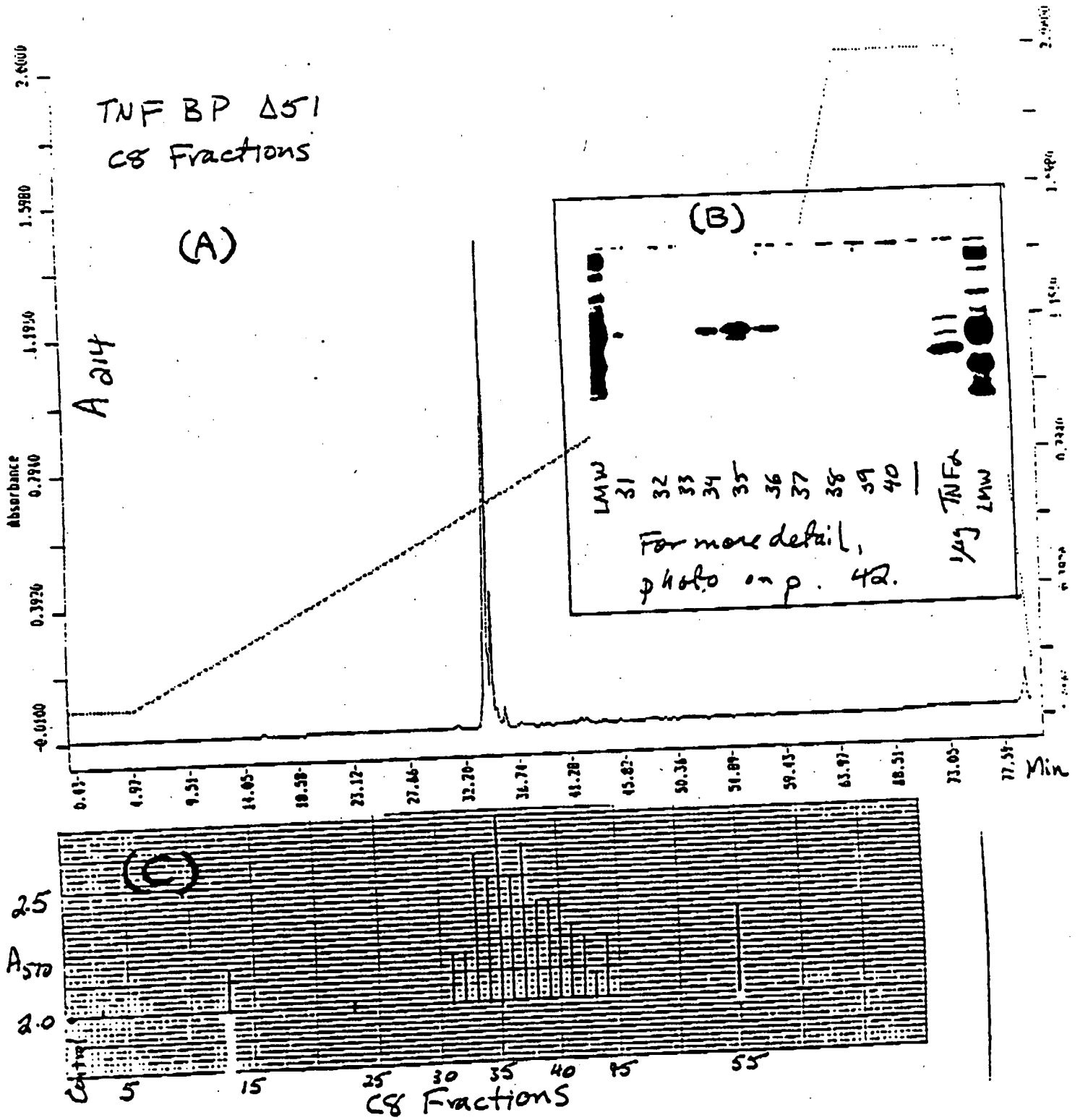


FIG. 45

